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ABSTRACT

This report is the result of three expert panels (on language and language impairments, balance and balance disorders, and voice and voice disorders) which met in 1994 and 1995 and reported research accomplishments, federal program goals, and research opportunities to the National Deafness and Other Communication Disorders Advisory Board. For language and language impairments it reviews the following: language in deaf and hard-of-hearing people, language and language impairments in children and adults, and comparative studies of language and language impairments. For balance and balance disorders, the report reviews public health and education; signal transduction and transmission; development, aging, regeneration and genetics; control of posture and balance; control of gaze; perception of spatial orientation and autonomic control; diagnosis; and treatment. For voice and voice disorders, the report examines: normal structure and function; aging; biomechanics; diseases and disorders of the larynx and upper aerodigestive tract; and application of technology to prevention, diagnosis and treatment. An executive summary presents an overview of all three areas. An appendix provides the text of Public Law 100-553, the National Deafness and Other Communication Disorders Act of 1988. Also appended is a list of panel members. (DB)

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NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and
Other Communication Disorders

National Strategic Research Plan

Language and Language Impairments

Balance and Balance Disorders

Voice and Voice Disorders

1994 - 1995

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Other Communication Disorders

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U.S. DEPARTMENT OF
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FOREWORD

The National Deafness and Other Communication Disorders Act of 1988 became Public Law 100-553 (Appendix A) on October 28, 1988, establishing the National Institute on Deafness and Other Communication Disorders (NIDCD) within the National Institutes of Health (NIH). The law required that the Director, NIDCD, establish a National Deafness and Other Communication Disorders Program and prepare a plan to initiate, expand, intensify and coordinate Institute activities concerning disorders of hearing, balance, smell, taste, voice, speech and language.

In response to this mandate, a Task Force of scientific experts representing the seven program areas of the Institute convened in January 1989 to prepare the first National Strategic Research Plan which has guided the Institute over its first few years. The National Strategic Research Plan is also intended to inform the nation's scientists of areas of opportunity for research and to provide them with guidance as they formulate their own research plans. The Plan informs persons with communication disorders and their support organizations of past research accomplishments and potential future activities. In addition, the Plan is intended to inform members of Congress of research progress and future research opportunities in scientific areas within the purview of the NIDCD.

Public Law 100-553 required the National Deafness and Other Communication Disorders Advisory Board to review, evaluate and update the plan periodically to assure its continuing relevance. To meet this legislative mandate, the National Advisory Board decided that it would update two of the six sections of the plan every year thus updating the entire plan within a three-year period. In 1994, the National Advisory Board reexamined its policy for updating the Plan and decided that it would be more appropriate to update one section every year, thus changing to a six-year cycle. The National Advisory Board established six subcommittees, one for each section of the Plan and made recommendations for expert panel members, compared the research portfolio of the Institute to the National Strategic Research Plan, identified changes in the field since the Plan was developed, recommended levels and areas of research activity and suggested potential initiatives.

In 1994, the National Advisory Board was deactivated as part of the Administration's effort to streamline the Federal government and the responsibilities of updating the Plan were transferred to the National Deafness and Other Communication Disorders Advisory Council.

The Expert Panel on Language and Language Impairments convened on January 19 through 21, 1994, the Expert Panel on Balance and Balance Disorders on March 2 through 4, 1994; and the Expert Panel on Voice and Voice Disorders on January 18 through 20, 1995. The results of their efforts are contained in this report. (Members of the expert panels are listed in Appendix B).

FOREWORD

The members of the expert panels are due special thanks for giving of their talents and time in developing this document. Their meetings brought together representatives of a broad array of scientific disciplines within the areas of language, balance and voice. The members of the expert panels shared their diverse ideas and worked diligently to achieve consensus on a comprehensive view of each field and a vision for the future. Subsequently, expert panel members refined their efforts with numerous revised texts.

Dr. Dorothy W. Aram and Dr. Eleanor M. Saffran, Cochairpersons of the Language and Language Impairments Expert Panel; Dr. Fay B. Horak and Dr. Joseph B. Nadol, Jr., Cochairpersons of the Balance and Balance Disorders Expert Panel; and Dr. Gerald S. Berke and Dr. Jerilyn A. Logemann, Cochairpersons of the Voice and Voice Disorders Expert Panel deserve special appreciation. The update to the National Strategic Research Plan is a product of their experience, expertise and guidance. Along with their fellow expert panel members, they have formulated a plan for future research in important scientific areas of the NIDCD.

James B. Snow, Jr., M.D.
Director
National Institute on Deafness and
Other Communication Disorders

PREFACE

The National Strategic Research Plan of the National Institute on Deafness and Other Communication Disorders (NIDCD) was first prepared in April 1989 and presented the research recommendations of more than 100 eminent scientists in the seven program areas of the NIDCD. These areas are hearing, balance, smell, taste, voice, speech and language. During 1991 to 1993, all six sections of the National Strategic Plan were updated and the second update cycle of the Plan began in 1994. This report contains the 1994 updates of the Language and Language Impairments and Balance and Balance Disorders sections and the 1995 update of the Voice and Voice Disorders section of the 1991-1993 plan.

The ability to communicate via language is essential to the psychologic, economic and social well-being of the individual. Millions of Americans have disorders that impede the acquisition of language or that disrupt language function after it has been acquired. The primary goals of research on language are to provide an understanding of these disorders and to develop strategies and interventions that will prevent these disorders or reduce their severity and improve the communication of individuals who do become language-impaired. These goals cannot be achieved without a fundamental understanding of the normal language system, which is being sought in studies of hearing children and adults, as well as in people who are deaf. Recent technological advances offer new avenues for studying the neural bases of normal and disordered language, which will contribute to this basic understanding and ultimately to the development of new treatment methods.

Disorders of the vestibular system can cause a variety of disabling problems, including imbalance, falls, dizziness, spatial disorientation, and blurred vision, which seriously interfere with many activities of everyday living and often make employment impossible. Although the precise incidence of balance disorders, disequilibrium and dizziness from vestibular disturbance is difficult to determine, it is clear that these disorders constitute a major public health problem. Basic and clinical research is needed to study normal and abnormal vestibular function, development and aging of the vestibular system and new approaches to improve the diagnosis and treatment of balance disorders.

The voice is the foundation for all spoken communication. A good voice is important in modern society because there is a great demand for effective spoken communication. Although most people take voice production for granted, reduction or loss of the ability to produce the voice can disrupt spoken communication and thus can have far-reaching personal, professional and social consequences. Although progress made so far has been promising, the opportunities for better understanding of the process and disorders of voice have barely been explored. These opportunities constitute a vital area of research that could benefit the lives of many individuals. The larynx is also involved in other critical functions that sustain life, that is swallowing and respiration. When swallowing is impaired in children or adults, there can be costly physiologic consequences including pneumonia and dehydration. Research on normal and disordered swallowing and respiratory functions and their relationships is needed in order to effectively evaluate and treat individuals with these disorders.

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PREFACE

The updates of the Language and Language Impairments, Balance and Balance Disorders and Voice and Voice Disorders sections of the National Strategic Research Plan have provided an opportunity to evaluate the progress that has been made in these areas in the past years and to assess future research needs and opportunities. The recommendations presented here are expected to lead to exciting advances in scientific knowledge and improve the quality of life for many people.

Dorothy M. Aram, Ph.D.
Eleanor M. Saffran, Ph.D.
Cochairpersons, Language and
Language Impairments Panel

Fay B. Horak, Ph.D.
Joseph B. Nadol, Jr., M.D.
Cochairpersons, Balance and
Balance Disorders Panel

Gerald S. Berke, M.D.
Jerilyn A. Logemann, Ph.D.
Cochairpersons, Voice and
Voice Disorders Panel

National Institute on Deafness and
Other Communication Disorders

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Executive Summary

Language and Language Impairments

The ability to communicate via language is essential to the psychologic, economic and social well-being of the individual. Millions of Americans have disorders that impede the acquisition of language or that disrupt language function after it has been acquired. The primary goals of research on language are to provide an understanding of these disorders and to develop strategies and interventions that will prevent these disorders or reduce their severity and improve the communication of individuals who do become language-impaired. These goals cannot be achieved without a fundamental understanding of the normal language system. The research program therefore encompasses basic research on language in all its modalities (spoken, signed and written). This includes the manner in which language is produced and understood, as well as the biological substrates of language and the processes through which children acquire language.

Language acquisition occurs naturally for most children, including those who can hear and those who are deaf with deaf parents who sign. Much has still to be learned about how this process occurs. While it is recognized that children come into the world equipped to learn language, the nature of the predisposing capacities remains unclear. The environmental requisites for language acquisition also need further examination. These are likely to include cultural, ethnic and social factors. In light of the diversity of the U.S. population, it is important that the various subgroups be properly represented in the subject pools for studies of language. Some individuals with normal hearing, as well as those with hearing impairment, have problems with language comprehension and/or production that are sufficient to interfere with interpersonal communication. In young children, these disorders often involve difficulty in the acquisition of the ambient spoken or signed language and may result in impairments of reading and writing. In older children and adults, brain injury can result in the loss of previously achieved language skills.

Language disorders affect children and adults differently and pose different sorts of research questions. In the case of the child whose language development is abnormal from the outset or who sustains impairment in childhood, the disorder occurs in the context of a language system that is not fully developed. Language impairment in the adult is the result of damage to neural systems that are likely to be less malleable. Therefore, while the broad goals of research on language disorders are similar whether the affected individuals are children or adults, the research agendas for these two populations are considered separately.

The review of recent research accomplishments and the discussion of research opportunities are divided into three general areas: language among deaf and hard-of-hearing children and adults, language and its disorders in children and language and its disorders in adults.

Among deaf and hard-of-hearing children and adults, several different languages and/or different modalities are used. This creates major questions with respect to language choices and the means to achieve language acquisition and communicative competence, as well as the achievement of literacy in English. Major advances have been made in understanding language acquisition and use for the approximately five percent of deaf children born to deaf parents who learn American Sign Language (ASL) as a native language. Recent research has shown that these children acquire ASL in a manner analogous to acquisition of a native spoken language in hearing families. It has also been shown that the linguistic structure of natively acquired ASL is grammatically complex and equivalent in richness to spoken language and that the brain areas subserving language are similar for ASL and spoken languages. For the remaining 95 percent of the deaf population born to hearing families, language exposure and acquisition is highly heterogeneous and is complicated by factors such as age of identification and intervention, parental response, language use in the environment, attitudes toward deafness and additional factors that affect hearing children as well, such as socioeconomic status and cultural factors. Concerns about literacy have prompted research on reading and writing of people who are deaf. There has been particular interest in studying those who have become successful deaf readers of English. This work indicates that successful deaf readers process English similarly to successful hearing readers. It also appears that the grammatical errors made by these deaf readers are similar to those of hearing learners of English as a second language. Among the hard-of-hearing population, recent research has focused on the role of assistive listening devices for the acquisition of both oral and written English.

Language disorders in children who do not have impaired hearing may be observed in the comprehension and/or production of syntax and morphology, vocabulary and phonology, as well as in the use of language for social discourse. Some children with language disorders have concomitant difficulties such as pervasive cognitive, perceptual and/or motor processing problems that interfere with language learning. Other language disorders in children may be attributed to demonstratable brain injury sustained before or during language acquisition. These are, therefore, acquired language impairments. A third group of children exhibits language deficits in spite of grossly normal nonverbal intelligence and hearing and motor development. These are referred to as children with specific language impairment (SLI). The etiology of SLI is unknown although a number of hypotheses are being investigated including genetic/familial, neural-developmental and environmental contributions, as well as possible cognitive, perceptual and motor differences. Most research recognizes that there are complex interactions among these factors and that multiple etiologic factors may contribute to SLI. SLI children have been found to have difficulty with multiple aspects of language. In particular, however, they have been shown to have substantial difficulties acquiring morphology and syntax, findings which have led to investigation of language-specific mechanisms and of interactions between deficient information processing abilities and features of the linguistic system. Valid and reliable assessment instruments are now available for making use of parents' knowledge of early language and communicative development, although these instruments will need further refinement for use with culturally and linguistically diverse groups. Language intervention research with children has focused upon identifying factors that improve the effectiveness of language remediation. Longitudinal research on children with SLI has demonstrated that children with persistent language difficulties are at risk for reading and other academic difficulties as well as for social and behavioral problems.

Adults with previously normal levels of language function may become language impaired as a result of insults to the brain. Focal brain lesions, due to stroke or head injury, are the primary cause of such disorders. Language deficits also occur in the context of progressive degenerative disorders, such as Alzheimer's disease. In both cases, the previously normal language system may be altered in ways that can be devastating to the economic and social well-being of affected individuals. Although the symptomatology of these disorders has been known for more than a century, their functional and neurogenic bases are not yet adequately understood. In recent years, however, examination of these disorders in light of theories of normal language processing has begun to provide a new understanding of aphasic symptoms in terms of the disruption of specific types of linguistic processes, and these findings are leading to the development of new approaches to assessment and remediation. Further insights are emerging from comparative research involving English and other languages. In addition to providing data on the vulnerability of various language structures to brain damage, these studies of signed as well as spoken languages are addressing such basic issues as the nature of hemispheric specialization for language. Finally, the development of new techniques for imaging brain structure and function is providing a more adequate basis for determining not only the neural correlates of language disorders and the substrates for normal language processes, but also for examining the possibility of the reorganization of language function after brain injury.

In all three areas of investigation, it is recognized that intervention for language impairments must be predicated, and its success evaluated, on the precise knowledge of the ways in which the condition differs from the normal state. Current research opportunities emphasize the importance of understanding the normal language system, in addition to clarifying the ways in which language function or its acquisition can break down. This knowledge will open new avenues of intervention and remediation.

Language in Deaf and Hard-of-Hearing People

Language Development in Deaf and Hard-of-Hearing Children

There is great variation in the acquisition of spoken and/or signed language by deaf and hard-of-hearing children. Although some children become very proficient, others do not. Overall, there is a need to study the language abilities of deaf children who differ in their communication skills, and the relationship of those abilities to the nature and timing of the learning experiences provided by parents and teachers.

There is some evidence that, if other variables are held constant, deaf children of deaf parents may tend to outperform other deaf children on a variety of academic and psychosocial measures. No full explanation is yet available of this phenomenon, which requires further study.

Studies are needed of normal patterns for the acquisition of ASL and their relation to cognitive and psychosocial development in deaf children of deaf parents. In addition, to understand the normal patterns of such development, it is necessary to pursue parallel studies of disordered courses of development of signed language in the same population.

Since deaf children of deaf parents constitute only about five percent of the population of deaf children, it is imperative to achieve a better understanding of the typical patterns of language development of deaf children of hearing parents.

In addition, because hard-of-hearing children constitute a substantial portion of the population and because even minimal hearing impairment can affect the acquisition of language, it is imperative that a better understanding be developed of the typical patterns of language development of hard-of-hearing children.

Finally, because many deaf and hard-of-hearing children come from African-American, Hispanic-American or other minority group families, special attention should be given to language acquisition in these linguistic and cultural settings. Within this area, then, new studies are needed to:

- Identify and describe how deaf infants communicate nonlinguistically with their parents and how the transition is made from nonlinguistic to linguistic communication.
- Identify and describe the patterns of acquisition of ASL and manually coded English systems for children who are native learners, and also for children who are exposed to ASL and manually coded English systems at a later age and/or from an incomplete source. Studies should include all regional and ethnic dialects of ASL.
- Identify and describe the patterns of language acquisition of children exposed primarily to manually coded English systems.
- Identify and describe the patterns of language acquisition of children exposed primarily to oral language, either alone or in conjunction with Cued Speech. These studies should include particular attention to hard-of-hearing children, whose oral language success and/or problems need further documentation.
- Determine the outcomes of bilingual acquisition by deaf children, for whom ASL is acquired as a first language and English as a second language. It is also necessary to study other combinations of communication systems and the ability to switch among them when appropriate.
- Identify the critical periods for both the natural acquisition of and training in spoken or signed language of deaf and hard-of-hearing children, and describe the effects of delayed exposure to language on linguistic competence and cognitive and academic abilities.
- Identify and describe the invention of gestural language systems by children without formal sign input and the relation of this process to eventual signed or spoken language development.
- Identify and describe the processes of language change that occur when multiple languages are in contact with each other (pidginization) and when

languages are acquired from imperfect input (creolization). These reorganizational processes are thought to occur widely in the families and classrooms of deaf children and adults, due to the varieties of English, ASL and other forms of signing used, but are not yet well understood.

- Examine the language environment of deaf and hard-of-hearing children with hearing parents and teachers, and examine its impact on language acquisition, including the quality of the language model provided by the parents and teachers.
- Develop nonbiased assessment materials and procedures to evaluate deaf children in the full range of areas of communicative competence, as well as cognitive nonlinguistic skills. Special care must be taken to ensure that these materials are appropriate for children from a variety of cultural, ethnic and linguistic backgrounds.
- Develop culturally appropriate procedures for identifying and treating deaf and hard-of-hearing children who have language disorders.
- Study the effects of new technology and intervention strategies (such as auditory prostheses, computer-based training systems and holistic teaching methods) and the age at which they are applied for promoting language acquisition by deaf and hard-of-hearing children.

Studies of Literacy in Deaf Children and Adults

- Examine the nature of processing words, sentences and texts, with emphasis on successful versus less successful deaf and hard-of-hearing readers, in an attempt to identify the most effective reading strategies. Such studies should include readers from a variety of cultural backgrounds.
- Investigate the relationships among speech processing, sign processing and literacy.
- Examine the interaction of acquisition of signed languages with spoken and written language and begin to characterize the resulting bilingualism. Studies of the order of acquisition of speech and signed languages as it affects children's eventual acquisition of English language and literacy should also be conducted.
- Assess the role of captioning, telecommunication devices, personal computers and other technologic influences and teaching methods in the improvement of the literacy skills of deaf and hard-of-hearing children.

Finally, no widely accepted writing system for ASL exists. However, there is a growing unwritten ASL literature (including stories and poems), akin to oral history in unwritten spoken languages, that can provide a source of knowledge regarding literary forms, conventions and styles for the deaf child. Because this area has not yet been studied, research is needed to:

- Explore the efficacy of teaching ASL literacy to provide a base for the development of English literacy in deaf children.

Basic Research on Sign Language Structure and Function

Although much progress has been made in understanding the structure of ASL, there are still several topics that require extensive research. In addition, further research is needed on comparative sign language analyses. ASL is used primarily within the United States and in some parts of Canada; in other parts of the world, distinct and quite different sign languages are used, for example, British Sign Language, Japanese Sign Language, etc. This situation presents an opportunity to examine similarities and differences among the sign languages of the world for purposes of theoretical understanding of spoken and signed language universals and understanding how educational sign methods can make the most natural use of the visual-gestural modality. Research is needed to:

- Study further the structure of ASL, particularly its syntax and semantics, including the full range of ASL dialects used by American deaf people from varying regional, ethnic and cultural groups. Included should be studies of the nature of ASL "creolization."

- Study natural signed languages used in deaf communities in other countries, in comparison to ASL, to determine universal principles and dimensions of variations across signed languages.

- Investigate the underlying perceptual and motor processes necessary for controlling a signed language, particularly as they may differ from the nonlinguistic processes relevant to spoken language due to the complex nature of space and movement in a signed language. Research is needed in both adults and children.

- Continue to study the processing of ASL, isolating the component operations and their time course, for both native and nonnative signers.

Finally, research is needed to identify and characterize the neural systems that underlie the representation, perception, and production of signed languages, in both adults and children. Major questions concern the degree to which cortical organization is similar or different for spoken and signed languages, and the ways in which cortical organization may be changed by age of acquisition and by early perceptual and linguistic experience. Research is needed to:

- Continue investigation of which brain areas are employed for sign language processing, using event-related brain potential (ERP) techniques as well as newly developing imaging technology, such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET).

- Study how the neural organization of basic sensory systems and their resulting function may be changed by deafness and/or by exposure to sign languages, considering the effects of the age at which these changes occur.

- **Characterize more fully the effects of brain injury, and other known causes of language impairment, on sign language comprehension and production. Further careful study of sign-language aphasia in native signers is of particular interest.**

Language Impairments in Children

Etiology

- **Identify prenatal exposures in combination with environmental experiences that predispose children to language disorders.**
- **Determine which language disorders are genetically transmitted. Examine the modes of transmission and seek to identify genes, through molecular genetic techniques, associated with language disorders.**
- **Identify environmental factors associated with language disorders, and document their impact through the developmental period.**
- **Examine the neural substrates of perceptual, motor, cognitive and linguistic deficits in children with developmental language disorders using new technologies involving neuroimaging techniques, neurochemical methods and animal models.**
- **Examine the interplay between early learning and environmental experiences, language development and related neural systems.**

Symptomatology

Although important advances have been made in detailing the symptomatology of language disorders in children, much of this work has described language characteristics at a single point in time and has not addressed developmental or comparative issues. Considerable work needs to be done on how to differentiate more effectively between language differences and language disorders and how language disorders are manifested within different cultural and linguistic groups. Recommendations for continued work are to:

- **Pursue developmental studies of the unique characteristics of the language of children with language impairment and in particular perform comparative studies of these linguistic characteristics across languages, cultures and clinical populations.**
- **Specify further the contribution of such factors as perception, cognition and motor function to the development and use of linguistic knowledge in children with language disorders.**
- **Determine the degree of comorbidity between language disorders and dyslexia, other learning disabilities, attention deficit disorder and psychopathologic disorders.**
- **Develop computer models to test theories of normal and disordered language and reading development.**

Assessment

- **Establish the validity of diagnostic measures to identify language** disorders using a variety of criteria such as etiologic factors, linguistic features and educational progress or social outcomes across the developmental period.

- Develop assessment tools to identify more accurately language disorders in children of different socioeconomic groups or whose primary language is other than English.
- Assess language performance and develop alternatives to normative procedures that will differentiate between language variations and disorders at different ages across socioeconomic, linguistic and cultural groups to identify ways of more appropriately serving these populations.
- Develop and study the efficacy of assessment procedures that examine the development of information processing abilities including nonverbal cognitive skills in children with language disorders.
- Establish more adequate normative standards for language development among children who develop more than one language or dialect.

Intervention

- Develop and test the efficacy of new intervention strategies that apply theoretical models of language acquisition and processing that have been shown to be valid in predicting normal and abnormal language acquisition.
- Investigate how etiologic and symptomatic categories interact with remediation strategies across cultural groups (including children living in poverty) to determine how to tailor teaching methods to the specific language learning needs of individual children.
- Test the effect of various intervention strategies on children in multilingual environments. These strategies might include teaching exclusively in either the native or second language, teaching some language aspects in one language and others in the other, teaching both languages simultaneously and teaching the two languages sequentially.
- Examine the efficacy of augmentative and alternative communicative systems to teach oral and graphic language and to improve the communication skills of persons with severe communication impairment.

Outcome

- Identify those factors that can be relied upon to predict persistent disorders of language.
- Study the bases for the relationship that has been found or hypothesized between language disorders and psychosocial, behavioral, vocational and academic outcomes.
- Describe the economic and social cost of language disorders.

- **Develop valid and reliable outcome measures to determine the efficacy of intervention.**

Language Impairments in Adults

Analysis of Processes Underlying Language and Language Impairments

- **Further refine and implement techniques ("on-line" methods) that are sensitive to the structure and time course of normal language processes.**
- **Develop "on-line" techniques that are appropriate for use with a range of clinical populations.**
- **Compare and contrast the structure and operation of language processes within the oral, written and signed modalities.**
- **Describe further the forms of impairment that occur within these modalities.**
- **Elucidate the relationship between language ability and nonlanguage perceptual, cognitive and motor skills in normal adults.**
- **Distinguish between deficits that may be specific to the language system from deficits attributable to perceptual, motor or other cognitive disorders and clarify the distinction between them.**
- **Develop computer models that simulate normal language and its disorders.**

Brain-Language Relations

- **Study the neural systems that underlie language processing in normal subjects. This research will require the further development of certain neuroimaging techniques, for example, ERPs, fMRI, magnetic evoked fields (MEF) and the use of various isotopes with PET, to study the metabolic and physiologic basis of language processing in normal subjects. The success of these efforts will depend as much on the design and interpretation of the cognitive tasks that are used in conjunction with these imaging techniques as on the sensitivity of the imaging methods themselves.**
- **Use electrocortical stimulation and single-cell recording techniques to investigate brain-language relationships, where such techniques can be applied in appropriate individuals.**
- **Study variability in the neural systems that underlie normal language use and the determinants of that variability. These determinants may include gender, age, genetic factors, social factors, multilingualism and others.**
- **Study the nature of the lesions associated with language disorders in adults, including their location, size, etiology and evolution over time. These studies will require quantitative analyses of lesions identified through computerized tomography (CT) and MRI and exploration of the functional consequences of these lesions using PET, fMRI and ERP.**

- **Explore the implications of new findings on neural plasticity for the recovery of language functions after brain damage in adults.**

Assessment, Intervention and Recovery

- **Revise and improve existing assessment procedures to update them to current understanding of the nature of normal language processing and its disorders.**
- **Develop assessment instruments that are valid for different cultures, linguistic groups, ages, genders and socioeconomic status levels.**
- **Develop assessment tools that reveal the linguistic and nonlinguistic communicative abilities of language-impaired subjects in natural situations.**
- **Develop assessment tools that measure the effects of language impairment and its treatment on the quality of life of individuals.**
- **Investigate the efficacy and efficiency of existing approaches to treatment. Such studies should include assessment of treatment directed toward improvement of language impairments, developing mechanisms to compensate for language impairments and improvement of functional and pragmatic abilities.**
- **Develop and evaluate computer-assisted instruction as an intervention strategy for language-impaired subjects. These studies should include exploitation of recent advances in computer systems, including interactive compact disc (CD) and CD-ROM (read only memory) technology.**
- **Develop and evaluate alternative and augmentative communication systems for adults with language deficits.**
- **Investigate the potential role of pharmacologic treatment as adjuncts to rehabilitative intervention in language disorders.**
- **Explore methods that can maintain and prolong language function in individuals with progressive degenerative diseases.**
- **Identify and test the validity of variables that can be used to predict improvement and/or response to treatment.**
- **Identify the optimum amount, intensity and duration of treatment for acquired language disorders in adults.**
- **Investigate means, for example computer-assisted methods or the use of volunteers, to provide efficacious treatment at a reduced cost compared to traditional management.**

Comparative Studies of Language and Language Impairments

- **Obtain normative data from healthy individuals of various ages to characterize changes throughout the lifespan in patterns of language use.**

- Continue comparative analyses of disorders in different languages and dialects on the assumption that language-specific differences in symptoms can help reveal the universal linguistic and cognitive mechanisms that subserve language processing.

- Perform normative studies of language and its disorders in individuals who speak more than one language or dialect. Relevant issues may include the age at and order in which the speaker's languages were acquired, the contexts in which those languages are used, the impact of code switching (that is, mixed use of two or more languages in a single situation) and variations in cognitive style and mode of processing that can be observed in multilingual children and adults.

- Obtain basic epidemiologic information on the incidence and prevalence of and risk factors for language disorders within African-American, Hispanic-American, Asian/Pacific Islander-American, Native-American and other minority group populations, as available data may not be generalizable across these groups.

- Within and across cultural and linguistic groups, assess the impact of socioeconomic status and gender on the incidence and prevalence of language disorders, including recovery and efficacy of treatment, as well as attitudes toward such deficits by relevant cohorts of individuals within these groups.

- Compare and contrast the profiles of language impairment and associated deficits that are observed due to different causes (for example, congenital versus acquired impairments; focal versus diffuse brain injury; specific language disorders versus language impairment in the context of mental retardation and/or progressive dementia).

These challenges can be met only through the collaborative efforts of different disciplines and institutions. This statement is increasingly true for every science, but it is especially important for the study of language and language impairments because languages come in so many varieties and serve so many social, political and cultural functions. For this reason, a high priority should be given to initiatives that bring scientists together around a set of common goals – to develop new tools, to establish conventions for the use of those tools, to establish patient registries and to build joint archives of behavioral, neurologic and demographic data from disordered populations.

Balance and Balance Disorders

Disorders of the vestibular system can cause a variety of disabling problems, including falls, imbalance, dizziness, spatial disorientation, and blurred vision, which may seriously interfere with many activities of everyday living and often make employment impossible. Disorders of the vestibular system can have serious consequences to safety, such as motor vehicle accidents and job injuries. It has been estimated that up to 50 percent of falls in the elderly may be due to vestibular disorders. Indeed, falls in the elderly may be responsible for many of the 200,000 hip fractures that occur annually in Americans over the age of 65 years with a combined medical and surgical cost for patient care in excess of $8 billion per year. For individuals over the age of 75 years, disequilibrium is the most common single symptom presented to primary care physicians. Disorders of balance are common in children and adults. For example, up to two-thirds of children with acquired deafness also have vestibular deficits.

In addition to the sizable cost of diagnosing and treating individuals with vestibular disorders, the cost due to the loss of time from work is also significant. Balance disorders also exact a military cost. It has been estimated that approximately 30 pilots and their aircraft are lost per year because of pilot disorientation and subsequent error. Similarly, two-thirds of all astronauts experience significant motion sickness that can reduce their effectiveness in the first three days of orbital flight.

A better scientific understanding of balance disorders and more efficient and exact strategies to diagnose and treat these disorders are critically needed.

This report addresses the principal areas of research for balance and balance disorders. One of these is public health and education for health professionals and the general public. The true incidence of balance disorders is difficult to determine because of the lack of diagnostic criteria and gaps in the scientific understanding of the underlying pathology and pathophysiology of these disorders. The current lack of understanding of balance disorders can also result in misdiagnosis and failed therapy. If the excessive, unnecessary suffering, dependence and social and economic cost associated with balance disorders are to be eliminated, more research is needed to determine the incidence and social effects of these disorders and to improve their diagnosis and treatment.

Another area of research addressed by the report is vestibular signal transduction and transmission. To understand how the vestibular system controls balance, it is first necessary to understand how the sensory organs transduce or convert head accelerations, the effective stimulus along with gravity to the vestibular sense organs, to electric signals and how these signals are transmitted to the central nervous system. In addition, understanding of the molecular and neurochemical mechanisms of transduction and transmission will lead to improved pharmacotherapeutics.

Development, aging, regeneration and genetics are additional areas of research addressed by the report. Considerable progress has been made in identifying genetic control of inner ear development. New methods are enabling the identification of genetic vestibular disorders in humans and may make it possible to treat and eventually prevent vestibular disorders. Understanding normal development is critical for understanding the mature system and for recognizing, preventing, or correcting developmental deficits in vestibular function. Age-related decline in vestibular function is known to exceed age-related decline in other sensory systems. Thus, vestibular system degeneration, combined with declines in other sensory and motor functions and adaptive mechanisms for balance, gaze, and spatial orientation, results in a major public health problems for the elderly population. The possibility exists for reversing balance deficits by finding methods to regenerate vestibular sensors but still requires much research.

Another area of research focuses on the main physiologic functions of the vestibular system: balance and posture control, regulation of locomotion and other volitional movements, coordination of eyes and head for stable gaze, and perception of spatial orientation with effects on autonomic function. The essential role of adaptive plasticity in normal function as well as adaptation for dysfunction of the vestibular system has been recognized. Over the last several years, there has been an increasing appreciation of the complexity of interaction of vestibular, somatosensory and visual information. There has also been emphasis on contextual influences upon balance, gaze, spatial orientation and cognitive control. The role of the vestibular system has been shown to depend upon the particular movements, specific environmental conditions, and even upon the mental set of human subjects. New computer models and new technologies for stimulating and measuring these complex systems are leading to new insights into vestibular function which can be tested experimentally. Critical for identifying and treating balance disorders and the associated symptoms of dizziness, visual instability, as well as nausea and autonomic signs of motion sickness, is the need for a better understanding of the role of vestibular function in a variety of motor behaviors and perceptions of motion.

The last area for research covered by the report is diagnosis and treatment of balance disorders. Advances in modern technology have made evaluation of the individual who has a vestibular disorder a quantitative science. Opportunities exist to develop new, improved and cost-effective ways to diagnose and evaluate individuals with balance disorders. Following the advances made in the diagnosis of specific vestibular disorders, the application of specific pharmacotherapeutic agents for peripheral and central disorders continue to evolve. A fuller understanding of the physiologic basis for pharmacologic, surgical and rehabilitative therapy for imbalance, visual instabilities and dizziness is needed. Also needed is a thorough evaluation of the efficacy, cost-effectiveness and long-term outcomes of surgical, medical and rehabilitative strategies to facilitate compensation, reduce vertigo and improve balance in individuals with vestibular deficits.

Thus, the first area of research focuses on assessing the public health problem, assessing the current approaches to balance disorders and improving the education of health professionals and the public. This will close the gap between current research and quality health care. The second, third and fourth areas of research emphasize studies that enhance the understanding of the normal balance system. At the same time, they call for clarifying mechanisms that result in imbalance and other symptoms of vestibular disorders. The last area of research focuses specifically on developing ways to improve the identification and remediation of balance disorders.

Public Health and Education

Improvements in diagnosis, treatment and prevention of balance disorders and their consequences require improvements in diagnostic criteria and testing and better understanding of the underlying pathology and pathophysiology of these disorders. Understanding the true prevalence and costs of the disorders depends on the development of these criteria and the education of both the public and health care professionals. Research is needed to:

- Develop clear and clinically useful diagnostic parameters for disorders of vestibular disturbances.
- Study the underlying pathology in human temporal bones and correlate the findings with vestibular disturbances during life to understand better the pathogenesis and pathophysiology of these disorders and to validate diagnostic criteria and treatment strategies.
- Provide epidemiologic data concerning the incidence and prevalence of balance disorders in the population, across the life span in both genders, based on clear diagnostic criteria.
- Evaluate the impact of balance disorders on daily activities and work performance in different age groups.
- Evaluate the association of balance disorders with other disease processes (for example, autoimmune disorders, visual and other sensory disturbances, arthritis, neurogenic and cardiovascular disease, obesity and psychogenic disorders).
- Evaluate the frequency of balance disorders caused by drug therapy for the management of other medical problems (for example, hypertension, diabetes and mental disorders).
- Study and compare the efficacy and cost effectiveness of different medical and surgical approaches to the management of balance disorders.
- Study the efficacy of educational paradigms designed to improve the diagnostic and management acumen of health care professionals, to improve public awareness of the causes, diagnoses, and treatment for balance disorders and the prevention of their consequences (for example, falls, fractures and motor vehicle accidents) and to influence policies for the construction of housing and health care facilities to prevent falls and injuries related to chronic balance disorders.

Signal Transduction and Transmission

To understand how the vestibular system controls balance, posture and eye movements and regulates locomotion and volitional movement, it is necessary to understand how the end-organs convert acceleration stimuli to electric signals and how these signals are transmitted to the central nervous system. In addition, understanding the molecular and neurochemical mechanisms of transmission within brain stem and cerebellar nuclei will help define functional circuitry and will lead to improved pharmacotherapeutics. Research is needed to:

Signal Transduction

- Determine the cellular and molecular mechanisms for active regulation of potassium, calcium and other principal ions in the fluid filling the bony vestibular labyrinth, the endolymph, and within the cells of the vestibular sense organs. Identify the organic constituents of endolymph. Investigate the mechanisms of hormonal regulation of the major ion transporting systems. Describe the mechanisms of bulk-water movement (caused by net secretion or absorption of solutes) across vestibular epithelial cells.

- Describe the motions of the endolymph and the overlying membranes of the vestibular sensory organs, the cupulae and otolithic membranes in response to applied forces associated with head acceleration. Characterize the attachment of the kinocilia and stereocilia to the cupulae and otoconial membranes. Determine the structural and biochemical features of ciliary bundles that shape their responses to applied forces. Measure the movement of hair bundles in response to physiologic stimuli. Determine whether forces generated by hair cells can influence the movement of accessory structures.

- Study molecular components of the transduction apparatus. Identify the proteins that constitute the apparatus, including the mechanically sensitive ion channel, the adaptation motor, the tip link and related connectors. Determine the role of the structural components of the stereocilia and the cuticular plate in transduction. Identify how these structures connect to each other and to the structure of the hair cell.

- Characterize the structural and biophysical properties of hair cells of different types and in different regions of the vestibular sensory tissues. Determine the contribution of hair cell basolateral ionic currents to the modification of the receptor potential and the control of neurotransmitter release. Study the ionic exchangers and the pump proteins in the membranes of hair cells.

Signal Transmission

- Use a combination of biochemical, pharmacological and molecular biological techniques to identify the afferent neurotransmitters released by hair cells and postsynaptic neurotransmitter receptors present in ascending nerve terminals of the ascending neural pathways. Investigate the possible existence of neuromodulators in hair cells and afferent nerve terminals that can modify afferent synaptic transmission. Determine whether there are novel modes of synaptic transmission between type I hair cells and calyx endings.

- Study the locations and characteristics of the ion channels in the afferent nerve terminals that are responsible for the conversion of synaptic depolarization to repetitive spike discharge. Localize the spike-initiation site in the terminal or parent axon using sodium-channel markers. Determine how spatiotemporal patterns of transmitter release, properties of afferent fibers, and efferent activity generate firing patterns of vestibular axons. Develop dynamic models that predict and explain patterns of afferent fiber activity on the basis of the anatomical and biophysical properties of end-organs.

- **Characterize the mechanisms of synaptic transmission, including peptide co-transmission, between efferent endings and their postsynaptic targets in hair cells and afferent dendrites. Learn the conditions that modulate the vestibular descending neural activity.**

- **Identify the transcription factors and immediate early genes that regulate gene expression of receptors and neurotransmitters involved in central and peripheral vestibular neurotransmission. Define alterations in gene transcription that occur as a result of vestibular disease or during compensation and adaptation.**

- **Employ modern techniques to identify vestibular system neurotransmitters and receptors (for example, in situ hybridization, polymerase chain reaction, subtractive hybridization and immunocytochemistry). These techniques should be utilized separately and in combination with classic neuroanatomic procedures to elucidate the neurotransmitters or receptors associated with individual vestibular neurons and specific vestibular pathways.**

- **Clarify the location and role of glutamate and GABA receptors in the neuronal organization of central vestibular circuits.**

- **Determine the cellular and subcellular localization of the neuropeptides and monoamines. Define their roles in central vestibular neuromodulation.**

Development, Aging, Regeneration and Genetics

A better understanding of neural development of the vestibular system, regeneration of vestibular sensors after loss, and genetic control of the vestibular system promises new breakthroughs in the treatment and prevention of balance disorders common in the elderly. The developing and regenerating system provides insight into the potential for neural plasticity and compensation following injury or age-related vestibular degeneration. New research is needed to:

Development

- **Identify transcription factors and trophic factors that are active at different stages of inner-ear and central vestibular development. Develop animal models, such as transgenic mice or zebrafish, in which factor expression can be manipulated.**

- **Understand the timing of cell maturation in the inner-ear and central vestibular nuclei. Understand how changing biophysical and molecular properties correlate with functional maturation.**

- **Characterize the stages of vestibular synaptogenesis, emphasizing central synapse formation and its timing relative to synaptogenesis in the periphery. Take advantage of species differences in developmental timing to resolve the temporal relations of synaptogenic events. Develop molecular and immune markers for different stages of vestibular synapse formation.**

- Develop in vitro vestibular end-organ preparations and continuous hair cell lines with which the development of cells can be observed over time. Use these to elucidate the factors regulating cell division and differentiation in the sensory epithelia.

Aging

- Determine the extent of functional vestibular loss that accompanies aging in humans. Investigate the relationship of the rate and extent of recovery to the age at the onset of vestibular dysfunction.

- Determine the anatomical and biochemical changes of the vestibular system associated with aging, including the quantification of cellular changes in the vestibular receptor organs, primary afferents (second-order vestibular nucleus) neurons, and motor efferent elements.

Regeneration and Genetics

- Develop in vivo models for vestibular sensory end-organ regeneration. These models should further the understanding of synaptic plasticity and the development of treatment strategies for vestibular disorders.

- Investigate the mode of action of suppressor genes that prevent the development of vestibular schwannomas. Determine whether tumor formation can be caused by inactivation of the normal allele of the NF2 suppressor gene.

- Identify human families and new transgenic mouse lines with specific vestibular dysfunction. Locate the defective genes with linkage analysis and identify the genes.

- Investigate familial differences in the vestibular effects of aminoglycoside ototoxicity and identify the underlying genetic differences.

- Develop herpes virus and adenovirus vectors for the delivery of genes into the inner ear and brain stem. Understand which cells can be targets of such vectors. Identify promoters for genes expressed in specific cell populations to increase the specificity of gene targeting. Develop animal models of genetic defects that can be used to test the effectiveness of gene therapy.

Normal/Abnormal Vestibular Function: Posture, Gaze, Locomotion, Other Volitional Movements and Motion Perception

New scientific studies have the potential for understanding the various roles of the vestibular system in posture, gaze, locomotion, other volitional movements and motion perception at both the cellular and subcellular levels as well as at the natural behavioral level. There is now recognition that vestibular function needs to be studied not only in terms of fixed reflexes, but also as an integral part of complex sensory motor behavior. There is a need to understand how the role of vestibular information in posture, gaze, locomotion, other volitional movements and motion perception can change or adapt, depending on context and higher level function such as attention and intent. Some research needs, such as identifying neural elements and mechanisms for adaptation and higher level control, apply equally well to vestibular control of posture, gaze, locomotion, other volitional movements and motion perception, whereas other research needs address issues specific to each vestibular function. New research opportunities in posture, gaze, locomotion, other volitional movements and motion perception are needed to:

- Characterize the structural, biophysical, pharmacological, cytochemical and molecular properties of neurons in different vestibular reflex circuits. Such characterization should be done in animal models and in vitro preparations in which neuron projections are identified to the greatest possible extent.
- Establish the influences of somatosensory, visual and auditory inputs, as well as motor signals on neurons in the vestibular pathways. This should include the influences of sensorimotor context and cognitive variables, such as attention.
- Determine the patterns of convergence of multiple sensorimotor signals in the central vestibular nuclei and the functional associations with other neural circuits and behavior.
- Determine the distribution and organization of otolithic organ and semicircular canal inputs to the vestibular nuclei, cerebellum and related brain-stem targets. Relate these findings to their roles in animal motor behavior.
- Establish the neural sources, targets and characteristics of signals that modulate the vestibular control of eye movements, head stability, balance and spatial perception on a moment-to-moment basis. This would include effects of sensorimotor context, viewing distance and viewing angle.
- Determine behavioral, perceptual and cellular response characteristics during complex combinations of linear and angular motion and interactions with other sensory inputs relevant to spatial orientation, balance and vestibular reflexes.
- Define the role of otolith organs in the vestibular control of eye, head and body movements during linear and complex (combined angular and linear) motion, especially those produced during (or resembling) natural motor behaviors such as locomotion.
- Extend the development (1) of mathematical models to include experimentally testable models of vestibular pathophysiology as well as normal function and (2) of general models for posture, gaze and motion perception in normal and artificial environments.
- Establish the behavioral characteristics and underlying cellular structures and mechanisms that govern adaptive changes in vestibular pathways. Define the specific sensory cues required for their acquisition.

- Identify the specific sensory signals that trigger and govern adaptive modification of vestibular reflexes and behavior and define their temporal processes. Consider visual and auditory signals relevant to spatial localization and somatosensory cues that supply information about body orientation.

- Determine whether adaptive capabilities can be exploited experimentally to modify the behavioral sequelae of aging and disease.

- Examine the potential relationships between adaptive processes and the more rapid, context-dependent modifications in vestibular pathways and behaviors.

- Expand the understanding of adaptive plasticity in vestibular reflexes and spatial orientation to include responses to linear and angular acceleration. This should include how signals convey target position, influence vestibular neurons and maintain calibration.

- Examine the cellular and molecular mechanisms that underlie adaptive plasticity and compensation in vestibular reflexes to understand fully the adaptive process. This undertaking requires analysis of alterations in gene expression, transcription, post-translational modification and second messenger systems. This investigation should clarify whether such changes are responsible for alterations observed in adaptive changes.

- Conduct anatomic and physiologic experiments to determine the pattern of vestibular inputs to the cerebral cortex. Study the integration of vestibular with other inputs in these areas.

- Study modulation and control of vestibular reflexes and behavior by higher centers, including the upper brain stem, cerebellum and cerebral cortex.

- Develop computational models that explore the neural basis of vestibular behaviors and of sensorimotor transformation relating vestibular information and postural coordination. Develop dynamic models of spatial orientation that incorporate consistent and conflicting multisensory inputs and allow for adaption.

Control of Posture and Balance

- Characterize the circuits that link neurons to vestibular motor systems. These studies should emphasize the pathways involved in the vestibular control of neck, axial and limb muscles, including intrinsic and commissural pathways in the vestibular nuclei and spinal interneuron networks involved in vestibular reflexes and behaviors.

- Characterize the sensorimotor strategies, neural mechanisms and adaptive patterns underlying postural control during a wide variety of natural activities and under varying environmental conditions.

- **Identify the compensatory strategies used by healthy and vestibular-deficient subjects to adapt to novel sensory and mechanical conditions while preserving equilibrium and postural alignment. Investigate the capacity for sensory substitution to compensate for abnormal or missing vestibular function, to assist in postural stability.**

- **Identify the role of head stabilization in space for coordination of complex body movements. Identify the role of the vestibular system, and vestibulocollic reflexes in particular, in head stabilization.**

Control of Gaze

- **Determine the extent of linkage and independence between vestibulo-ocular and vestibulospinal signals in the central vestibular neurons, particularly those involved with eye/head coordination. Identify the nonlabyrinthine influences on these cells.**

- **Determine the effect of gravitational force on the control of head and neck movement and postural stability.**

- **Expand the understanding of adaptive plasticity in the vestibular control of gaze during linear and angular (rotational) head movements. Include how signals conveying visual target position influence vestibular neurons and how they maintain calibration.**

Perception of Spatial Orientation and Autonomic Control

- **Combine measures of spatial orientation and motion perception with physical indices of eye, head and postural movements during tilt and linear acceleration in normal subjects and in individuals with well-diagnosed vestibular disorders.**

- **Use the free-fall environment of space flight to extend investigations of human spatial orientation and motion perception in the effective absence of gravity.**

- **Characterize the effects of vestibular signals on individual respiratory muscles, on blood flow to different vascular beds and on the neurons that control cardiovascular and respiratory function.**

- **Explore the effect of various cerebral cortical lesions on spatial orientation perception in humans and animal models.**

- **Study the relationships among the perception of orientation, the putative internal model and automatic postural orientation mechanisms.**

Diagnosis

Opportunities exist to develop new, improved and cost-effective ways to diagnose and evaluate individuals with vestibular disorders. Such techniques can also be used to evaluate the natural history, diagnostic criteria, results of treatment and objective and subjective functional outcomes in individuals

with a variety of types of vestibular and balance disorders, including those attributable to trauma, disease, hereditary and degenerative processes. Research is needed to:

- Develop and evaluate new ways of testing semicircular canal and otolithic organ function, including the use of active versus passive motion. The study of freely moving subjects and the application of galvanic stimulation should employ both postural and ocular motor tests. Build normal and abnormal quantitative vestibular testing databases for valid interinstitutional comparisons.
- Develop tests of the contribution of proprioceptive inputs, including neck receptors, to gaze and balance function.
- Develop portable, ambulatory, noninvasive and telemetric methods of recording and monitoring horizontal, vertical and torsional eye movements, to evaluate individuals with intermittent disturbances of vestibular function.
- Develop improved psychophysical methods for evaluating disorders of perception of the orientation and motion of the head and body, to quantify dizziness and disorientation.
- Develop animal models to establish the reliability, validity and limitations of vestibular tests.
- Develop better laboratory methods to detect immune-mediated and hereditary vestibular disorders. Use brain-imaging techniques for assessing the structural and functional correlates of peripheral and central vestibular disorders.
- Develop tests that exploit central adaptive capabilities and compensatory strategies to predict outcomes in individuals who have vestibular disorders and who are treated with medical, surgical or rehabilitative therapies.
- Employ epidemiological and statistical methods to analyze the results of vestibular function tests in individuals with vestibular disorders. Design questionnaires about subjective symptoms and the ability to perform the activities of daily living. Such studies will help define diagnostic criteria, psychologic and sociologic impacts, natural history, subjective outcomes and objective responses to therapy.
- Determine the pathologic bases of vestibular disorders using studies of the temporal bones of individuals with well-defined clinical histories and examinations and laboratory testing results.

Treatment

A full understanding the normal neurochemical basis of balance and vestibular function is needed for the development of pharmacologic agents that can be used to treat individuals with balance disorders. Also needed is a thorough evaluation of the efficacy, cost-effectiveness and long-term outcomes of surgical, medical and rehabilitative protocols in facilitating compensation, reducing vertigo and improving balance in individuals with vestibular deficits. Regarding various forms of therapy, research is needed to:

Medical Therapy

- Isolate, clone, sequence, characterize and map the genes responsible for peripheral and central neurotransmission in the vestibular pathway.
- Determine the site and mechanism of action of currently used pharmacotherapeutic agents for vestibular disturbances and motion sickness.
- Determine the effect of pharmacotherapeutic agents on vestibular adaptation.
- Determine the relationships between balance disorders and psychological dysfunction and the effects of medical treatment on each.
- Improve the efficacy and specificity of intratympanic instillation of gentamicin, including the development of delivery systems and new vestibulotoxic drugs and vectors for the selective chemical ablation of the vestibular end-organs in intractable vestibular disturbances.
- Develop agents active in facilitating vestibular regeneration as well as in selectively destroying diseased vestibular end-organs and the means for their delivery to the inner ear.

Surgical Therapy

- Study the efficacy of surgical procedures for the management of Meniere's disease, including endolymphatic shunt procedures, using prospective, controlled clinical studies.
- Study and compare the efficacy and cost-effectiveness of the medical and surgical management of balance disorders.
- Develop anatomic or electrophysiologic methods to accurately separate the vestibular and cochlear nerves during a vestibular neurectomy.

Rehabilitative Therapy

- Understand the effects of treatment at the pathophysiologic, impairment, functional limitation and disability levels. Develop outcome measures for assessing treatment efficacy, including balance, quality of life, functional independence and prevention of falls.
- Develop new approaches to using biofeedback, novel technologies and sensory substitution strategies to improve function with rehabilitation intervention.
- Quantify functional performance and other changes related to vestibular rehabilitation intervention compared with or combined with medical or surgical intervention.
- Assess the value of treatment using reliable outcome measures that demonstrate changes in balance impairment and function.

Voice and Voice Disorders

Normal Structure and Function

The larynx and pharynx are key structures in the upper aerodigestive tract which participate in three vital functions: respiration, swallowing and voice production. The voice is the foundation for all spoken communication. Although most people take voice production for granted, reduction or loss of the ability to produce the voice can disrupt or preclude spoken communication and thus can have far-reaching personal, professional and social consequences. A good voice is important in modern society because there is a great demand for effective spoken communication. The voice box (larynx) acts as a valve between the pharynx (throat) and trachea (windpipe) and, along with other structures in the region, serves as the gatekeeper between the respiratory and digestive systems. The primary structures for voice production are the vocal cords or folds. The voice is produced by bringing the vocal folds close together and exhaling. When air pressure from the lungs reaches a sufficient level, the vocal folds are blown into vibration, causing the air flow from the lungs to become pulsed. The pulsed air flow is further modified by vocal tract shaping which occurs above the larynx and is perceived as sound. The pharynx, oral cavity and nasal cavities alter the sound thus producing speech. The respiratory system provides the energy source and is coordinated with the larynx and upper aerodigestive tract during voice production.

The second important role of the larynx is protection and regulation of the airway. During a cough, the vocal folds close while the expiratory muscles of the chest and abdomen contract to expel mucus or foreign material from the tracheobronchial tree.

The same upper aerodigestive tract structures involved in voice and speech production are also active during a third function, swallowing. During swallowing, the larynx is elevated, moved forward and closed tightly allowing food or fluid to move into the esophagus. The pharyngeal walls contract top to bottom and the tongue base moves rapidly backward to propel food efficiently past the closed airway and into the esophagus.

Information from many disciplines such as acoustics and speech perception, engineering, gastroenterology, neurology, otolaryngology and speech-language pathology will be required to improve the understanding of the complex nature of laryngeal and pharyngeal function and their actions during respiration, swallowing and voice production.

Anatomy, Cellular and Molecular Biology and Genetics

- Study the anatomy of vocal control by using noninvasive imaging in human subjects.
- Use molecular and cellular biological, neurochemical and immunocytochemical techniques to study species-specific neural circuits in the human brain that control voicing, including the definition of asymmetries in the cortex and subcortical structures that are related to voice production.

- Use molecular and cellular biology to study peripheral motor, sensory and autonomic innervation of the human larynx.
- Study the structure and biomechanics of the laryngeal muscles with special emphasis on the identification of muscle subunits (compartments).
- Study the molecular specializations of laryngeal muscle fibers, nerves and soft tissues.

Development and Lifespan Alterations

- Use molecular expression studies to define the role of genetic factors in normal and abnormal laryngeal development better.
- Use aerodynamic, acoustic, kinematic and electrophysiologic techniques to study the normal development of voicing control mechanisms and to specify age- and sex-related differences in vocal function.
- Continue to delineate the effects of hearing impairment and cochlear implantation on vocal control, with special emphasis on identifying critical periods for vocal learning and rehabilitation.
- Conduct epidemiologic studies on the effects of lifestyle (for example, diet, smoking, exercise, alcohol consumption and drug use) and culture on laryngeal function.

Gender, Lifestyle and Cultural Influences

- Study gender differences in the effects of hormones on the larynx.
- Study gender differences in susceptibility to voice disorders.

Role of Auditory Feedback in the Development and Maintenance of Vocal Control

- Analyze critical periods for habilitation and rehabilitation of vocal control in individuals with hearing impairment.
- Study vocal changes in prelingually and postlingually deaf individuals who have had cochlear implants.

Aging

- Attain a better understanding of the process of cell death and the ways in which it influences the vocal and swallowing function with aging.
- Study the effects of selective neuronal death in the brain stem on the control of voice production and swallowing.
- Identify the basic pathogenic mechanisms underlying age-related degenerative processes in the highly specialized muscles of the larynx and upper aerodigestive system.
- Study the cellular biology of cartilage and joint deterioration as it effects

voice production and swallowing in aging.

Muscle Atrophy

- **Study the pathogenic mechanisms of age-related degenerative processes in laryngeal muscles.**

Deterioration of Joints, Ligaments, Membranes and Other Tissues of the Laryngeal, Pulmonary and Secretory Systems

- **Study further the biomechanical properties of laryngeal cartilages, ligaments, muscles and mucosa.**
- **Study the mechanical characteristics of the laryngeal joints with special emphasis on attaining a better understanding of the ways in which the cricoarytenoid joint functions in vocal fold opening and closing.**

Biomechanics of the Larynx and Upper Aerodigestive Tract during Vocalization, Respiration and Swallowing

Biomechanics of the Larynx

- **Study the influence of the vascular supply and mucosal fluid layer on vocal fold vibration.**
- **Determine the essential elements required for vocal fold oscillation, with a goal toward developing a neolarynx from autologous tissues.**

Control of Pitch, Loudness and Vocal Quality

- **Continue studying mechanisms of pitch, loudness, quality and register control using both humans and comparative models.**
- **Delineate the acoustic-to-perceptual transformation with special emphasis on identifying those aspects of the acoustic signal that give rise to the perception of various voice qualities, particularly disordered voice quality.**

Vocal Tract Component Interactions

- **Continue to increase research emphasis on the control and timing of laryngeal behavior in coordination with respiratory and articulatory activity.**

Swallowing

- **Conduct more research on the effects of various bolus types and on using various voluntary controls on systematic changes in laryngeal and pharyngeal function during swallowing.**
- **Collect more information on normal infant swallowing, including details concerning the influence of structural maturation on the swallowing function's transition from infant to adult mechanisms.**
- **Continue efforts to develop nonradiographic methods for evaluating swallowing function.**

- **Determining the details of peripheral and central neural control of swallowing.**

- **Establish a database on the anatomy of human swallowing structures, including the exact innervation of each muscle, the internal structure and biomechanics of such structures and the distribution of sensory structures.**

Comparative and Theoretical Models of Voicing

Comparative Models

- **Delineate species-specific differences in voice and swallowing structures and functions through the use of comparative studies.**

Computational Analysis, Modeling and Speech Synthesis

- **Improve the accuracy of computationally based laryngeal models, perhaps through the use of finite element approaches.**

Exceptional Vocal Behavior

- **Continue to study exceptional vocal behavior (for example, in singers), with particular emphasis on mechanisms of vocal control and efficiency, predisposing factors for superior vocal performance, vocal endurance and aging effects.**

- **Investigate the nature, variability and the effects of overuse on the professional speaking and singing voice.**

Diseases and Disorders of the Larynx and Upper Aerodigestive Tract

Disorders of the larynx and pharynx are very common and affect everyone at some time in their lives. When disease disrupts an individual's swallowing or voice production, the consequences can be devastating to the health, well-being and livelihood of the person.

Because of their anatomic location, high-frequency vibration during voice production and rapid function during swallowing, the vocal folds, the larynx and the pharynx have been difficult to examine and study, a fact that has delayed research on these important structures in the past. Increased knowledge and new means of analyzing laryngeal and pharyngeal function including improved imaging have greatly enhanced scientists' ability to understand the disorders that affect the vocal and swallowing mechanisms. Progress made has been promising, but the opportunities for better understanding of the disorders of voice and swallowing have barely been explored. These opportunities constitute a vital area of research that should lead to improved lives for many individuals.

Population- and Outcome-Based Research

- **Promote vocal health awareness in the public.**

- Develop data on prevention, diagnosis and therapy of voice disorders. These data are needed on the incidence, prevalence, risk factors and outcome measures of therapy for congenital and acquired voice disorders. These studies should include measures of dysfunction and disease severity and development of a staging system for evaluating common voice disorders.

- Determine the effects of age, gender, race and culture on the incidence, prevalence and outcomes of treatment for diseases and disorders of voice production and swallowing, including cultural differences in diet, health care, behavioral patterns and lifestyle, as well as individual factors.

- Determine the effects of environmental factors on disorders of voice production and swallowing.

- Conduct epidemiologic studies into misuse and abuse disorders, including prevalence, risk factors, environmental effects and efficacy of treatment and management.

- Conduct population-based longitudinal studies. There are only limited data available on the capability of the vocal folds to withstand the demands of daily voice use without injury. The impact of voice loss in certain professions is much greater than others. Preventive maintenance of vocal health in highly vocally demanding professions may be an alternative to the more traditional delivery of health care.

- Efficacy studies should be conducted on the various diagnostic tools available for laryngeal function testing. Currently there are multiple laryngeal function measures that may have diagnostic validity. There is a need for the establishment of commonly agreed upon clinical guidelines for application of these tools in evaluation of affected individuals.

- Investigate the outcome of methods used for prevention, early diagnosis and therapy for specific disorders. There is a need to establish a cost-effective, high-quality approach to treating the various disorders of the vocal system. The costs of the assessment must be balanced by the likelihood of benefits. The establishment of these guidelines may be based on meta analyses or other large multi-institutional collaborative studies.

Congenital and Acquired Structural Lesions

Congenital Abnormalities of the Larynx and Vocal Tract

- Study the genetic and molecular basis for laryngeal and upper aerodigestive tract disorders. These studies should include research on genetic and environmental interactions in congenital abnormalities.

Neoplasms

- Determine the molecular basis for malignancy of the head and neck. Important progress has been made in identifying markers that may reflect key factors in the control of malignant transformation of cells. Extensive studies will be required to define the natural history of malignant cell progression in the vocal tract. Research is needed to define the prognostic value of particular markers before broad screening programs can be considered.

- Investigate chemopreventive agents. Thousands of individuals who are at high risk of developing laryngeal carcinomas are now candidates for chemoprevention protocols following curative therapy for a primary head and neck cancer in an attempt to diminish the likelihood of their developing a second one. The effects of current and new chemopreventive agents on the larynx are unknown, but the action of such agents is an important area of research.

- Conduct studies that refine and develop the most effective means of treatment of laryngeal and pharyngeal cancers, as well as of other common laryngeal disorders. They should include basic research on the factors that control epithelial cell differentiation and growth, (for example, interaction of retinoids with their receptors) and how these factors are disturbed in carcinogenesis. Studies also are needed to understand and modulate immune functions in this disease. Long-term research should assess recurrence rates, effects of treatment, the effects of cofactors such as smoking and voice abuse and chronic laryngeal irritation.

- Conduct carefully controlled objective analyses of the results of therapeutic options for treatments of carcinoma of the larynx. Approximately 50 to 75 percent of all individuals with head and neck cancer in the United States receive radiation as part of their treatment. Yet there is relatively little information available regarding the effects of irradiation on laryngeal function. However, with the advent of advanced techniques for laryngeal study, measurements of vocal fold vibration and analysis of acoustic parameters, there now exist opportunities for more objective analysis of radiation effects on the larynx.

Viral Infections

- Investigate mechanisms whereby intrinsic and extrinsic factors interact with viruses to modify cell growth and differentiation to cause benign and malignant neoplasms.

Inflammatory Disease of the Vocal Tract

- Study the processes of inflammation and wound repair specific to diseases of the vocal and swallowing systems. This research should include studies of pathophysiology, prevention, detection and intervention.

- Design studies to produce new methods of diagnosis and new treatments for inflammatory diseases of the vocal tract, including infectious and allergic disorders. There is need for research on better diagnosis, assessment and treatment of chronic laryngitis and its relation to gastropharyngeal reflux. Long-term studies of the effects of chronic laryngitis should assess the impact of this disorder.

Trauma, Wound Healing and Treatment of Scarring

- Develop basic information on the management of trauma and wound healing, including laryngeal surgery and the sequelae of airway maintenance with endotracheal intubation and tracheostomy. These studies should include research on pathophysiology, prevention, assessment and treatment to maximize function.

- Conduct studies of scarring. A serious unsolved problem in the care of individuals with acquired scarring of the larynx after surgery or after trauma is glottic, subglottic and tracheal stenosis. The molecular factors involved in wound healing and scar tissue contracture are not understood. There is a need for research on better methods of airway support and stenting during the healing process. Research is also needed on better means for preventing trauma to the larynx and trachea from endotracheal intubation.

Neural Lesions and Disorders

- Conduct research into the pathophysiology of neural lesions that result in disorders of voice production and swallowing. This work should include neuropharmacologic and behavioral studies, studies of differential impairment across motor systems, nerve-regeneration studies, identification of markers for early diagnosis and research into dystonias and dyskinesia.

Peripheral Disorders

- Carry out additional clinical trials to determine the efficacy of surgical procedures to improve the ability to diagnose and treat these life-threatening conditions. Studies should include the investigation of vocal fold augmentation, thyroplasty, arytenoidectomy, cordotomy, selective reinnervation and electrical pacing.

- Conduct nerve-regeneration studies, needed as a basis for understanding the pathogenesis of peripheral disorders and for developing new forms of treatment. Molecular biologic studies of nerve regeneration are needed for a better understanding of idiopathic neuropathies that involve the larynx.

- Conduct research on laryngeal transplantation. Laryngeal transplantation is being explored in experimental animal studies. Major problems such as the appropriate reinnervation of abductor and adductor muscles have been recently approached. However, immune problems remain to be overcome before laryngeal transplantation can become feasible.

- Conduct research to evaluate the contribution of behavioral treatment to improve the voice source independently or in combination with surgical intervention.

Central Disorders

- Determine the efficacy of current diagnostic and therapeutic procedures for both peripheral and central disorders that affect voice production and swallowing and develop new approaches to these disorders. This research should include examining the efficacy of voice therapy for neurogenic disorders.

- Continue modification and refinement of the role of voice treatment for Parkinson's disease. Emphasis on the role of phonatory source enhancement and generalization to untreated articulation should be explored. Long-term evaluation of the treatment carryover in relation to disease progression is warranted. Application of this voice treatment to other neural disorders should be addressed.

- Clarify the relationship between neuropathology and laryngeal and pharyngeal disorders. Emphasis should be placed on early diagnostic markers and quantifiable differential aspects of neurogenic disorders and disease progression.

- Evaluate the relationship between limb and laryngeal manifestation of disease and response to neuropharmacologic and neurosurgical treatment. Preliminary data support differential manifestation across these diverse systems. Research should address the relationship between these systems of motor control.

- Conduct studies on dystonias. Focal dystonias of the head and neck cause disruption of speaking and swallowing and impair the quality of life. Advances in understanding dystonias (such as spasmodic dysphonia), derived from brain imaging and autopsy studies suggest that dystonias are attributable to brain lesions or biomechanical changes in the basal ganglia. Epidemiologic and case-control studies are needed to identify possible causative factors leading to the onset of this disorder.

- Continue modification and refinement of the use of botulin toxin injections into laryngeal muscles to reduce abnormal patterns of laryngeal muscle activation. Emphasis on optimal dose and placement of injection (which vary among individuals) will produce better guidelines on standards for treatment. Long-term evaluation of this treatment is needed to determine factors affecting efficacy with repeated injections. The mechanism of diffusion of the toxin in tissue should be better understood.

- Explore alternative methods of treating laryngeal dystonias, such as selective deinnervation of the thyroarytenoid muscles.

- Study respiratory dyskinesia (paradoxical vocal fold motion). This disorder is a problem that has recently been identified as a separate entity sometimes associated with asthma. The dyskinesia may affect vocal fold musculature, or any muscle group in the oropharynx. The mechanism for initiation of dyskinesia and the specific structures involved must be better documented. Characterization of specific parameters such as imaging studies with concurrent data on heart rate and pulmonary function are needed to define the nature of this disorder better. In particular, these disorders associated with asthma may be exercise or environmentally induced. Cross-disciplinary studies of these disorders are essential.

Systemic Disorders Affecting the Larynx and Upper Aerodigestive Tract

- Study the effects of systemic disorders such as connective tissue diseases, abnormalities of keratins and disorders of the lower respiratory tract, that negatively impact voice production and swallowing. Such studies should include basic research in pathophysiology and research on current and new methods of management and treatment.

- Study the effects of drugs on the vocal system and swallowing. There has been little direct research on the effects of drugs on the voice or on the interaction of drugs with other forms of vocal therapy, such as surgery or behavioral management. However, pharmacologic agents can negatively affect the voice and swallowing. For example, some blood pressure medications cause severe coughing. Other agents that increase or decrease secretions of the mucous lining of the larynx and upper respiratory tract can impair both voice production and swallowing. Antidepressants cause dry mouth. Anecdotal evidence implicates anti-inflammatory agents or topical corticosteroid sprays in the pathogenesis of vocal fold polyps. There is increased use of immunosuppressing drugs, some of which cause fluid retention in tissues. The effects of chemoprevention agents on vocal tract function should be studied. Further research also is needed into the impact of these and other agents on the vocal system.

- Conduct research into hormonal effects on the vocal system function. Imbalances of hormones may have a potent impact on the vocal system, particularly for professionals who rely on the quality of their voice. Hormonal imbalances can alter the distribution of electrolytes and water within the extracellular compartments of the vocal folds, causing them to become edematous or swollen and changing the characteristics of their vibrations. These changes occur with hypothyroidism, premenstrual syndrome, androgenic hormone-producing ovarian tumors, pregnancy and puberty in boys. They may follow the administration of birth control pills and postmenopausal hormone therapy in women. Studies are needed to determine the underlying molecular mechanisms of these problems and to clarify the best strategies for evaluating and treating affected individuals.

- Study the effects of specific keratin dysfunctions on voice production and swallowing. Genetic disorders of keratin synthesis or function alter the stability of epithelial cells. Even mild contact with the epithelium can cause blistering. Although generally thought of as skin disorders, the keratin disorders also affect the mucosal epithelium.

- Investigate disorders of connective tissues. These disorders clearly have an impact on vocal fold movement, but their effects on the laryngeal function are not well understood. Research is needed to define mechanisms of abnormal function and the best ways to deal with the problems it causes.

- Study problems of the lower respiratory tract (those airway structures below the vocal folds), that directly affect voice production. Emphysema and other pulmonary problems limit the airflow available for phonation. Evidence suggests that a variety of airborne pollutants may contribute to bronchial and laryngeal spasm and to changes in the mucous lining of the lower respiratory tract. Detailed analyses of mechanisms underlying the effects of diseases and disorders of the lower respiratory tract are needed.

Psychogenic Disorders of the Larynx and Upper Aerodigestive Tract

- Conduct research to set standards for counseling skills for voice therapists and develop guidelines for referrals to professional psychotherapists. Future investigative efforts in the area of psychogenic voice disorders should recognize the limited current academic training of speech/voice therapists and scientists in abnormal psychology and the psychotherapeutic process. The understanding and use of subtlety, semantics and interpretation skills, as well as displacement and projection of stress are important elements in successful voice therapy and investigation of the use of psychodynamics in voice therapy. Increased knowledge of these skills would be a helpful precursor to research planning.

Misuse and Abuse Disorders

- Conduct studies to achieve a better understanding of the basic anatomy and physiology of the voice-production mechanism and of alterations that occur during vocal misuse and abuse. These studies should include anatomy and histology in elucidating the mechanisms of injury and healing.

- Investigate the tissue-specific effects of chronic edema on the layered structure of the vocal fold as occurs in polypoid degeneration and chronic laryngitis. With the increase in prevalence of asthma in the general population (although abuse may be incidental or compensatory in these individuals), studies should be undertaken to find ways to determine the contribution of compensatory behaviors and reduce their overlay.

- Develop self-monitoring devices that can prevent vocal injury.

- Investigate the effects of pharmacologic agents on the vocal fold mucosa, as well as the effects of toxic agents both in the workplace and in the general environment.

- Conduct additional studies of epidemiologic factors, including prevalence of these disorders. In addition, there should be continued collection of a qualitative and quantitative database for physiologic variables influencing phonatory patterns.

Influencing Variables

Multicultural

- Study of multicultural factors in the etiology, pathogenesis, prevention, diagnosis and therapy of voice disorders.

Aging

- Collect better data on the prevalence of specific voice disorders and contributing factors associated with aging. Research is needed to understand why, in certain populations, children may be at greater risk for voice disorders such as hoarseness, vocal nodules and papillomatosis. Data are needed on environmental influences, personality characteristics and physical behaviors that contribute to voice disorders in children and senior citizens.

- Identify all age-related voice changes and contributing factors, such as change in respiratory support, diet, nutrition, physical and mental health, vocal hygiene and exercise (for example, singing).

- Evaluate the efficacy of voice treatment in reversing and limiting age-related changes in voice. Such work should evaluate the generalized effects of physical conditioning programs as well as specific treatment directed to laryngeal function for their impact on age-related changes in voice. The mechanisms underlying these changes should be studied.

- Determine the influence of the ingestion of certain medicines frequently prescribed in the later years of life on the vocal abilities of senior citizens.

Environment

- Identify environmental toxins by geographic areas and occupations to improve diagnosis and treatment.

Application of Technology to Prevention, Diagnosis and Treatment

There has been steady improvement in technology applicable to molecular and clinical research on disorders that affect voice, swallowing and respiration. There has been continued improvement in the technology used to image the upper aerodigestive/vocal tract and electrically measure its function in health and disease by utilizing multimodality applications. In addition, new surgical techniques and devices have been developed to improve the voice and alter voice quality. Further improvements in speech analysis, synthesis and recognition should further improve technology transfer to industry and improve the clinical application for people with voice disorders. Pharmacotherapeutic and behavioral control regimens are important areas in treating individuals with voice and swallowing disorders. Finally, recognition of the effects of systemic disease, medication, smoking and environmental hazards on voice and swallowing function has led to improved efforts of prevention.

Electromyography

- Develop better electrodiagnosis of voice and swallowing disorders for monitoring disease status and therapy.

Acoustic Signal Analysis

- Develop new techniques that provide an accurate and detailed profile of voice signals that are critical to voice quality and its disorders.
- Establish a comprehensive database of both normal and disordered voices to facilitate the development of acoustic signal analysis-based technology.

Imaging

- Determine the range of normal and abnormal laryngopharyngeal behavior for swallowing in terms of timing and magnitude of structural movements.

Augmentative and Alternative Voice Sources

- Develop new technologies, such as surgically implantable devices, to augment communication and swallowing after injury or disease.
- Encourage the use of multimedia technology for the enhancement of augmentative communication.

Surgical Technology

- Develop new surgical technology to improve minimally invasive surgery.
- Develop new technology that improves the intraoperative monitoring and prevention of iatrogenic injuries.

Aeromechanical and Respiratory Measures

- Obtain more information on the interactions among supralaryngeal, laryngeal, and respiratory structures in acute and chronic effects related to aspiration.
- Develop standardization of recording technology for acoustic, physiologic and imaging information.
- Improve and standardize techniques for measuring vocal disturbances and further investigate the origin and perceptual impact of these measurable vocal disturbances.

Behavioral and Medical Treatment

- Conduct multi-institutional, randomized clinical trials to determine the efficacy of behavioral and medical therapy for voice and swallowing disorders.
- Evaluate the impact of voice treatment on speech intelligibility in disorders of voice and speech production.

Biotechnology

- Provide information to clinicians and scientists for application of biotechnology to voice and swallowing.
- Improve technology transfer turnover; encourage and develop new application of technology useful for diagnosis and treatment.

Psychophysical and Perceptual Measures

- Obtain just noticeable difference (JND) data linking physiologic, acoustic and perceptual changes.
- Improve computer-synthesized productions of abnormal voice quality.
- Develop a database consisting of different types and severities of abnormal voice qualities that could serve as a standard for comparison across clinical and laboratory settings.
- Explore greater usage of computerized analysis-by-synthesis technology in linking abnormal voice qualities to perceptual ratings.

Measurement of Laryngopharyngeal Activity

- Investigate the magnitudes and timing of contact and fluid pressures occurring in the upper aerodigestive tract during normal and abnormal swallowing maneuvers.
- Obtain more information on peripheral and central nervous system control of swallowing behavior.
- Obtain additional information on the reliability and validity of noninvasive clinical procedures, such as cervical auscultation, in assessing swallowing disorders.

LANGUAGE
AND LANGUAGE IMPAIRMENTS

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Language and Language Impairments

Overview

Language is a uniquely human capacity that is fundamental to an individual's interaction with society and to social, political and cultural life. Although language usually is implemented through the auditory and vocal modalities, there are other means of exercising this basic capacity for symbolizing thought and of communicating these symbols to others; one such example is the development of signed language in deaf communities. The achievement of competence in a language within the first few years of life, which entails acquisition of a vocabulary of several thousand words and mastery of rules for the combination of those elements, must be regarded as one of the signal accomplishments of the species.

The failure to develop adequate facility in language due to developmental disability, or the loss of this facility due to brain insult, can be devastating. Those who are severely affected may be unable to lead independent lives; others may experience academic failure and limited employment opportunities. It is estimated that, nationwide, from six to eight million people have some form of language impairment. In addition to loss of livelihood, these disorders impose social isolation and personal suffering on the affected individuals and place a considerable emotional and economic burden on their families and on society as a whole.

These disabling conditions result from damage to the neural substrates for language or to the sensory systems that provide input to these neural mechanisms. In some cases, the effects of biologic limitations are exacerbated by failure to provide adequate environmental support for the acquisition of language. In many instances, however, the causal agents are not specific for language disability. Rather, the disorders are the result of conditions (for example, sensorineural hearing loss, stroke and traumatic brain damage, or metabolic or neurogenic dysfunction in the brain) that affect language more or less adventitiously and that are properly addressed in research programs that are specifically concerned with these conditions. The research agenda in the area of language disorders begins with the consequences of these agents for the language system. The agenda has as its major goal the development of prevention strategies, treatment strategies and other forms of intervention that can raise the level of language use -- written as well as spoken or signed -- of individuals with communication challenges to as functional a level as possible. These efforts, however, must be grounded in a fundamental understanding of the nature of the language code, of the manner in which such codes are processed, of the capacities that allow normal acquisition of language, and of the neural substrates that underlie the knowledge and processing of linguistic information. The research agenda therefore encompasses basic research on language impairments as well as research on intervention.

As presently understood, the processing of language begins, on the input side, with the recovery of linguistic units from auditory and/or visual signals and includes such operations as word identification, syntactic processing and sentence interpretation; processes on the output side include sentence formulation, word selection and programming of the articulatory musculature (vocal in the case of spoken language, manual in the case of signed language). Written language entails some of these same capacities, but requires different processes at both the input and output stages. Current psycholinguistic research is aimed at elaborating more finely grained models of these processes. In most adults, these operations depend primarily on the integrity of regions of the left cerebral hemisphere. Although this fact has been known for more than a century, it is only with recent technologic advances in imaging brain structure and activity that a more specific mapping of language components to neural components has begun to take shape. This effort is critically dependent on the increasingly detailed specification of language components that is emerging from research in the linguistic and cognitive sciences.

Thus the scope of the research program is necessarily a broad one, spanning a number of disciplines from linguistics to neuroanatomy and bringing a wide range of investigative tools from discourse analysis to experimental studies of language processing, from molecular genetic studies to the recording of brain electrical activity, to bear on the study of language and its disorders. Further complicating the task at both the basic and applied levels are issues of linguistic and cultural diversity. Although language function may depend on a core set of biologic capacities, it is acquired in a cultural context that must be taken into account in the assessment and treatment of language disorders. Given the cultural and linguistic diversity of the United States population, a single set of normative measures will not serve as an adequate benchmark for evaluating the communicative abilities of all individuals in society.

These diverse groups include Americans who are deaf, many of whom use a gesturally based language that requires separate description and distinct modes of evaluation and intervention; within this group there is also cultural diversity. Optimizing language acquisition for people who are hard-of-hearing is another research area with yet a different set of issues and methodologies. Longitudinally, the purview of the research program extends to the whole of the lifespan (and even beyond it, given the relevance of genetic factors to certain language disorders), from the perceptual-cognitive predispositions for language in infancy to the possible limitations on language capacity that may ensue with age. To a large extent, the issues posed by developmental language disorders and by language impairment that occurs in adults with previously intact language skills are different and call for distinct investigative approaches. In the case of a child with a developmental disability or with damage incurred postnatally, intervention is directed at a nervous system that retains a good deal of plasticity. In contrast, damage to the adult language apparatus disrupts a system that is less malleable, as well as one that is more highly specialized. The organization of this report reflects the different concerns and emphases of language research relating to these various populations.

Recent Accomplishments

Language Among Deaf and Hard-of-Hearing Children and Adults

In the United States, as many as 500,000 persons are born deaf or have lost their hearing before the acquisition of spoken language. Many of these individuals use a form of signed language as their primary mode of communication. Some use spoken English exclusively or in combination with signing. Research and services related to deafness must be concerned with the impairment of spoken language and with access to signed or spoken languages that are perceived visually.

An unknown but substantial number of additional people have a hearing impairment that is less severe but was present during childhood. These are people who are hard-of-hearing. Most of these individuals use spoken language as their primary mode of communication, although some also use a signed language. Despite the substantial benefit of auditory input to these individuals, their language acquisition is often characterized by difficulties not faced by people with normal hearing.

Americans who are deaf and hard-of-hearing reflect enormous diversity. Recent data suggest that approximately 40 percent of all people who are deaf and hard-of-hearing are under 18 years of age and are of minority status, with 17 percent being African American, 15 percent Hispanic American, and the remainder Asian/Pacific Islander American, Native American or "Other." Approximately two-thirds of deaf children are exposed to and use some form of manual communication, either English-based signing systems and/or American Sign Language (ASL). Recent evidence suggests that increasing numbers of hearing parents are using sign communication with their children. Hearing parents predominantly use English-based signing, but there is a growing interest in the use of ASL by hearing parents and siblings.

In short, several different languages and/or different modalities are used by deaf and hard-of-hearing children and adults. These languages may be learned at varying times of life, and predominantly from school environments or peers in addition to family, resulting in varying levels of skill. At the same time, Americans who are deaf grow up in a society in which the majority language is spoken English (with the possible addition of another spoken language in the home as well), and in which literacy must be achieved through the reading and writing of English. Thus, the major questions surrounding language in the deaf population concern language choice, the means to achieve language acquisition and communicative competence, and the means to achieve English literacy. The answers to these questions have been matters of some controversy, with shifts in dominant educational practices over time.

Major advances have been made in understanding language in one group of deaf individuals. Approximately five percent of deaf children are born to deaf parents and learn ASL as a native language, from birth, in the home. Recent research has shown that these children acquire ASL in ways analogous to the acquisition of a native spoken language in hearing families, going through normal stages of acquisition at appropriate ages. Further research has investigated the linguistic structure of ASL among these individuals as adults. Natively acquired ASL is grammatically complex and equivalent in richness to the spoken languages of the world. Recent work has shown that even the brain areas subserving language are similar for ASL and spoken languages. These findings have radically changed scientific views of the nature of language. Earlier views entailed the belief that language must be auditory-vocal, and that neural areas devoted to language were special to speech. As a result of the more recent findings, it is now widely recognized that normal language structure, acquisition and processing may occur in the visual-gestural modality as well, and that the language areas of the brain are not modality-specific.

In contrast to the deaf children of deaf parents, deaf children of hearing parents, who constitute the remaining 95 percent of all children who are deaf, have more variable circumstances surrounding early language acquisition. While some may have early exposure to signed language or may have adequate residual hearing to acquire some speech, others do not have a language model from which they can effectively acquire a natural language in the home. For these latter children, severe and profound hearing impairment often prohibits the effortless acquisition of spoken language, and the absence of signing skills among hearing parents prohibits the acquisition of a signed language. For these children, then, language exposure may be delayed, with teachers and/or deaf peers eventually providing them with linguistic input.

Several additional research findings have come from studying this population. First, research on communication within families in which signed language is not used and the deaf child fails to acquire spoken language has shown that such children may develop a "home sign" system, in which they devise a simple but language-like gestural communication system; however, it does not provide the child with a full and complete language. This finding has great scientific import, because it demonstrates the resilient linguistic abilities of the young child and indicates the need for further research in this area.

Second, there is a set of research findings that concerns the acquisition of ASL by deaf children of hearing parents at various ages beyond infancy. This research has shown that there is a critical period for the acquisition of ASL, just as there is for the acquisition of spoken languages by hearing individuals. The ability to acquire ASL diminishes as the age of the individual increases. As described above, in those exposed to ASL from birth, linguistic competence, sentence processing and even underlying neural mechanisms for language appear to be similar to those found in hearing native users of spoken languages. However, as in spoken languages, each of these seems to vary as a function of the age of first exposure to the language, with competence in and efficiency of processing ASL declining over age of first exposure, and with possible changes in neural organization for later learners. This research has both scientific and practical import, revealing previously unknown linguistic problems that may ensue from lack of early exposure to language.

Because deaf children of hearing parents receive their early language exposure either from school environments or from parents following the advice of practitioners, changes in this early language exposure depend heavily on how educators and medical personnel interpret the available research findings. Research on ASL has persuaded many such individuals that sign language exposure is necessary. However, there is also concern about the acquisition of English, which is of course the language of society at large and the language in which literacy must be achieved (there is no common writing system for ASL, and thus one cannot learn to read in ASL). The result has been that, while the majority of programs in deaf education have changed from oral methods to methods involving some type of signing, in most cases they do not use ASL. The majority of current programs (approximately 60 percent) employ signing systems that were invented to convey English structure and that are designed to enhance English literacy; only 40 percent are currently oral-aural (including one percent Cued Speech). Programs also vary in other aspects of instructional method, for example, whether the instruction is code-based or involves natural conversational immersion. Although some success has been claimed for each of these methods in teaching English to deaf children, the average reading and writing levels of the deaf high school graduate remain extremely low. In addition, recent research findings have shown that children exposed exclusively to the invented manual English signing systems develop idiosyncratic ways of signing that are unlike the structure of English and unlike the English signing systems to which they have been exposed. It has been argued that these systems include invented devices that are inappropriate for the visual-gestural modality, and may therefore not be readily learnable. In response to these problems, a small but growing percentage of new programs have begun to employ ASL as a language of instruction and teach English as a second language. The effects of such programs on linguistic competence and English literacy await additional years of use and research.

For the roughly 95 percent of the deaf population born to hearing families, then, language exposure is highly heterogeneous. It is additionally complicated by such factors as age of identification and of intervention, parental response, language use in the environment, attitudes toward deafness within the cultural group of the family, proficiency of the language models and factors that affect hearing children as well, such as socioeconomic status and cultural factors.

Because of concerns about literacy, some recent research has begun to focus directly on reading and writing by deaf people, particularly examining those deaf adults who are successful readers for clues to their methods of success. This research has indicated that successful deaf readers often process English using techniques similar to those of successful hearing readers, and that their grammar is often characterized by the same patterns of accuracy and errors as in hearing learners of English as a second language. Ongoing research is considering how these findings may be applied to the instruction of deaf readers who are not so successful.

In recent years, there has been growing research on language in the hard-of-hearing population. Because of this population's auditory abilities, research has focused on the role of assistive listening devices to the acquisition of English, both oral and written. This research has shown that the use of such devices for hard-of-hearing children may increase their ability to process spoken English in the classroom and may foster fuller participation in ongoing group activities at school. Further research is needed to delineate the potential of such devices for hard-of-hearing children.

A quite distinct area of study involves the mild or moderate hearing losses suffered by the aging hearing population, which is increasing in numbers in the United States. Recent studies of word recognition in this population suggest that central processing is worse than would be expected from peripheral hearing losses, indicating that there may be central auditory deterioration that requires further study.

Language and Language Impairments in Children

Language Development in Children

Any definition of abnormal language presupposes a definition of normality. For this reason, the study of language disorders in children is possible only to the extent that there is a clear understanding of the way in which languages are acquired by normal infants and children. It is necessary to know when various language abilities usually emerge, how they develop over time and how much quantitative and qualitative variation can be expected in healthy children. It is also important to know how language develops within different cultural contexts and within different languages and dialects.

Fortunately, great progress has been made in the last 10 to 20 years in the study of normal language development, with a particular focus on individual differences and the range of normal variability. By three to four years of age, most healthy children have acquired most of the grammatical structures and sound patterns of their language. The sequence in which these structures are acquired follows a typical course within which there is also room for individual differences in rate and sequence. As children enter school, they have to learn how to tell long stories, participate in conversations and use language to achieve a host of cultural and intellectual goals (which include reading and writing in literate cultures). From this point of view, disorders of language development can involve not only a failure to acquire specific kinds of linguistic knowledge (for example, phonological contrasts, grammatical structures and lexical items) but also a failure to develop the efficient, fluent and socially appropriate patterns of use that characterize an adult native speaker. Language and language disorders in childhood must be studied throughout the full range of development, from infancy to adolescence.

Recent advances have enhanced what is known about the brain systems that mediate language development in normal children. It is clear that these systems develop over a protracted period of time (that is, at least 15 years) and vary depending upon which aspects of language are measured. These results have implications for the description and remediation of childhood language disorders.

Language Disorders in Children

For most children, language is successfully acquired with relative ease in the span of a few years without formal training by adult caregivers. There are some children, however, who are challenged by the demands of language acquisition and as a result are unable to meet the communicative, educational and social expectations of their society. These children with developmental language disorders fall into many heterogeneous groups.

Language disorders may be evident in the comprehension and/or production of syntax and morphology, vocabulary and phonology, as well as in the use of language for social discourse. Some children with language disorders may have concomitant difficulties such as pervasive cognitive, perceptual and/or motor processing problems that interfere with language learning. Some may show a constellation of accompanying behaviors that lead to the clinical labels of autism or mental retardation. Other language disorders in children can be attributed to demonstrable brain injury sustained before or after the initial stages of language acquisition and therefore are acquired language impairments. However, a larger number of children exhibit language deficits in spite of grossly normal nonverbal intelligence, hearing and motor development. They have been referred to as children with specific language impairment (SLI). It is important that a research agenda address the needs of children in all these groups.

Although prevalence data need to be firmly established, it is estimated that approximately eight to twelve percent of preschool children have some form of language impairment. Several retrospective follow-up studies of SLI children have demonstrated that residual problems with language and language-related learning problems are often seen through adolescence and into adulthood.

Children with Specific Language Impairment

Many children with developmental language disorders are given the clinical label of specific language impairment (SLI). These children have normal hearing, score age appropriately on standardized tests of nonverbal intelligence and present no overt functional evidence of central nervous system damage. However, with the recent advent of new technologies that permit noninvasive in vivo neuroimaging, it has now been demonstrated that some SLI children show altered cortical and subcortical structures. Behavioral studies have revealed that these children perform poorly on perceptual, motor and cognitive tasks. Evidence is beginning to demonstrate that children with SLI have family members with language and reading disorders. Although United States prevalence data need to be more firmly established, preliminary estimates suggest that approximately five percent of preschool children fall into this clinical category and that males are nearly twice as likely to be affected as females. The absence of culturally and linguistically valid assessment instruments limits the precision with which prevalence data can be obtained from the demographically diverse population of the United States.

Etiology

The etiology of SLI is yet unknown. A variety of hypotheses concerning the basis of the language learning problems of children with SLI have been proposed. Some of these hypotheses are concerned with genetic/familial, neural developmental and environmental (prenatal and/or postnatal) contributions to SLI. Other hypotheses address possible cognitive, perceptual and motor differences that may contribute to SLI. Furthermore, most research recognizes that there are likely to be complex interactions among these factors and that there may be multiple etiologic factors contributing to SLI.

Current research suggests that in some children, SLI may be associated with a pattern of aberrant development of the cerebral cortex. There may be a specific deficit within the left hemisphere itself, or subcortical projections to this area, an abnormal state of cerebral asymmetry, or disordered interhemispheric integration. The mechanisms by and which neurogenic dysfunction occurs and the precise lesions that result in SLI are areas of active research interest with the ultimate aim of prevention.

Research in molecular genetics coupled with recent evidence of familial transmission of developmental language and learning disorders have led to studies of the heritability of language disorders. Studies are currently underway that use complex segregation analysis and twin designs to examine hypothesis of genetic transmission of SLI. These genetic studies may prove particularly powerful as a new tool for better defining phenotypic characteristics of SLI, as well as for providing the basis for molecular genetic linkage studies.

Biological and cultural environmental factors (pre- and postnatal) have been hypothesized to influence neural systems subserving language learning. The recent development of an animal model for investigating both structural and functional brain asymmetry may prove fruitful in advancing research in this area. Postnatal factors that may have impact upon language learning are currently under investigation. The level of language ability of the child has been shown to affect the parent's communicative interactions with the child, which has implications for future research, including computer modeling of the effect of interactions on language development.

Language Symptoms

Investigations of the language skills of SLI children have focused on syntax, morphology, phonology, semantics and pragmatics. They have revealed significant limitations in each of these areas. Although each language domain is acquired in a manner approximating normal development (albeit more slowly), the language profiles across areas often do not match those of younger, normally developing children. In particular, SLI children have been found to have substantial difficulties acquiring morphology and syntax. Efforts to explain this specific linguistic difficulty have either emphasized deficits in language-specific mechanisms or interactions between poor information processing abilities and features of the linguistic system. One approach to examining these hypotheses has been to study SLI children acquiring languages other than English, in particular, languages with different morphological features, such as Italian, Hebrew and German. These studies have demonstrated that the specific linguistic difficulties encountered by the children vary from language to language. Similar variations may occur across dialects of the same language. Other studies involving the direct teaching of invented morphemes to SLI children have demonstrated the role of inefficient processing in these deficits.

Neuropsychologic studies have revealed that children with SLI perform poorly on information processing and memory tasks. Subsequent research has demonstrated a significant correlation between the degree of nonverbal temporal processing disorders and both the pattern and degree of phonologic (perception and production) deficits in SLI children. Problems in phonologic awareness, as well as in awareness of other aspects of language, have been found to be highly predictive of reading problems among SLI children. Pursuit of these data offers a unique opportunity to integrate directly neurobiologic and behavioral/cognitive deficits that have been shown to characterize SLI children.

Assessment and Intervention

Valid and reliable instruments are now available for tapping into parents' knowledge of language and communicative development in children from eight to thirty months of age. Extensive norming information is also available on these measures, demonstrating substantial variability in rate and style of development in this age range. These low-cost parental reporting instruments have proven to be effective in screening and tracking the progress of children with significant disabilities. These instruments need further refinement, however, to make them more valid for culturally and linguistically diverse groups.

Language intervention research has identified certain factors that increase the effectiveness of language remediation. These factors appear to reflect enhancement of the opportunity to store and access phonologic units. In addition, teaching children to conceptualize phonemes appears to improve the language and reading decoding skills of SLI children.

Outcome

Prospective longitudinal research on children with SLI has focused on the preschool years. Studies have shown that two-year old children with fewer than 50 words and no two-word combinations are at serious risk of persistent language impairment, with approximately 50 percent of late talkers demonstrating persistent language problems through the preschool years. Children with persistent language deficits have been found to be at considerable risk for difficulties in reading and other academic skills, suggesting that SLI and reading impairment are closely associated. Furthermore, it has been shown that language and learning problems often persist into adolescence and adulthood. A few studies have addressed the social, emotional and behavioral concomitants of SLI. These studies suggest that children with SLI are at risk for social and behavioral problems, especially those involving attention and peer interaction.

Language Disorders in Children with Developmental Disorders

Language disorders result from a variety of conditions affecting cognitive development (for example, mental retardation), perceptual systems (for example acuity and information processing) and speech motor deficits. Mental retardation is a behavioral classification associated with a variety of causes that include genetic syndromes, disease processes, trauma pre- and postnatally and environmental influences. Many conditions that affect developmental progress are associated with general developmental deficits and may be associated with language disorders, including maternal substance abuse in pregnancy, fetal and infant malnutrition, lead poisoning, prematurity and congenital AIDS. Many of these children will be classified as mentally retarded. In the past, language learning in these children was thought to be a slow motion version of normal development. Recent research is beginning to document a variety of language learning outcomes that are unique to specific etiologies and different from those of normal children. Children with Down syndrome appear to have specific deficits in productive language compared to their language comprehension and nonverbal cognitive skills, with syntax more severely affected than vocabulary skills. Children with Fragile X syndrome appear to have more difficulties with semantics and pragmatics than with the acquisition of syntax and phonology. Girls with Turner syndrome and children with Williams syndrome appear to show strengths in language abilities compared with other nonverbal cognitive skills. Using language effectively for communication appears to be a particular problem for children with mild mental retardation, and these difficulties are not predictable from nonverbal cognitive skills.

Children with autism constitute another group for whom language is but one area of deficiency. Inadequate communication skills are the most common presenting symptoms, but nonlinguistic deficits are also an important component of this disorder. It is now clear that mental retardation is associated with autism in some children, but is not a defining feature of the disorder.

Children with motor deficits, (for example, cerebral palsy) appear to have deficits in language comprehension not attributable to their cognitive status. Due to a motor impairment, these children must depend on comprehension as their principal means of acquiring language. However, no studies have described language learning primarily through comprehension. Recent advances in assistive technology have resulted in augmentative and alternative communication devices using a variety of computer technologies. Studies are beginning to document dramatic improvements in communication abilities in persons with severe disabilities using a variety of augmentative communication systems. These devices provide opportunities for examining language learning in persons with severe cognitive and motor deficits. Of particular interest is research on alternative graphic representational systems and their impact on conventional learning of language and literacy.

Research involving children with language disorders accompanied by other developmental disabilities supports the view that insights into the basic processes of language learning may be enhanced by comparing the performance of different populations.

Acquired Language Disorders

Some language disorders in children occur after a period of normal development and are acquired through infections, tumors, stroke, trauma, epilepsy or head injury. Strokes in children are estimated to have an annual incidence of 2.52 per 100,000 children. Other causes, such as head injury, are estimated to be as high as 200 per 100,000 per year.

Advances have been made in specifying the relationship among acquired language deficits and the nature of central nervous system (CNS) involvement. Children with focal, unilateral lesions, such as those sustained following vascular episodes, generally have been found to have better long-term language development and recovery than children with lesions involving more diffuse brain structures, such as CNS tumors treated by whole-head radiation and chemotherapy, severe closed-head injury or epileptic aphasia. Both fluent and nonfluent aphasia may occur in children with acquired brain lesions, and a variety of syntactic and lexical comprehension and production deficits have been described following left-hemisphere lesions. However, delays in lexical development and in the development of syntactic structures have been documented following early lesions of either the left or right hemisphere, and delays in comprehension seem to be more common in children with right-hemisphere injury – an association that is not observed in adults. Attempts to relate language sequelae to lesion location within a hemisphere have been equivocal. Prognosis related to age at lesion onset is controversial and confounded by factors such as the diffuse nature of the lesion, concomitant seizure disorders and questionable premorbid status. Studies using electrophysiologic and neuroimaging techniques are beginning to address the nature of hemispheric reorganization following acquired language loss in children. Recent breakthroughs in developmental neurobiology using animal models have underscored the role of plasticity in early brain development and may help to shed light on the complex profiles of recovery and delay observed in children with CNS injuries.

Language and Language Impairments in Adults

Normal language development eventuates in a knowledge base and a set of processing components that ensure rapid and efficient comprehension of language as well as its fluent production. The adult language system can be compromised, however, by a variety of agents that affect the neural substrates for language function. Of those individuals who become language impaired, many are rendered totally dependent, although there is a wide range of possibilities for rehabilitation of communicative power and, in some cases, the return of economic self-sufficiency.

Current best estimates place at nearly one million the number of adults in the United States with acquired disorders of language due to stroke or traumatic brain injury. A large proportion of the estimated two million citizens with progressive dementing disease (Alzheimer's disease, Parkinson's disease) also have significant language impairment. Other conditions that impair language function include brain tumors and CNS infections (including AIDS). Some of these disease entities have a higher incidence and prevalence in specific ethnic groups (for example, the higher incidence of stroke in African Americans with sickle cell anemia). Language disorders are also found in adults who have failed to develop normal language because of childhood autism, hearing impairment or other developmental or acquired disorders of brain development.

In many cases, these etiologies affect all aspects of language and communication, but more specific deficits are also observed. For example, there are individuals who can read better than they speak, and a few who write better than they read. There are individuals who have enormous difficulty finding names for things but seem (at least superficially) to have control over other aspects of sentence structure. And there are others who can produce names for things but stumble over frequently used words such as "the," "is" and "of." According to some reports, there are individuals who are particularly impaired in naming animals and other living things, while others have specific problems with color words. Among bilingual speakers with aphasia, there are some who are most impaired in their second language, others who are more impaired in the language they acquired first. Many of these dissociations are controversial, but there is no doubt that language can break down in a variety of ways. The implications of these findings for alternative theories of the organization of language are being explored.

Understanding of the anatomic and physiologic bases of normal and disordered language has also progressed in recent years. This development has been facilitated by a variety of techniques for the structural imaging of the brain, including computerized tomography (CT) and magnetic resonance imaging (MRI), which offer information about lesion size and location that was once available only at autopsy. There are also tools for imaging the functional activity of the brain that make it possible to watch the living brain at work on a range of linguistic and nonlinguistic problems. For example, there are techniques to monitor brain metabolism and blood flow that use positron emission tomography (PET), single photon emission computed tomography (SPECT) and functional magnetic resonance imaging (fMRI). The functional organization of the language system has also been studied using magnetic evoked fields (MEF) and event-related brain potentials (ERP). Intraoperative electrocortical stimulation and cortical stimulation via subdural electrode grids have been used to identify specific areas of the brain in which stimulation interrupts performance on linguistic and/or nonlinguistic tasks. Electrocorticography and extra-cellular recordings from single cells in response to language stimuli have also been utilized during neurosurgical procedures. Transcranial magnetic stimulation is another new technique that has been applied to the study of the neurobiology of language.

The interpretation of results obtained with neural imaging techniques depends critically on the nature and quality of the behavioral data that are linked to neural structures and events. In this regard, the theories and methods of modern cognitive science have brought about important refinements in the understanding of processes that underlie normal and abnormal language functions. These new methods and insights have added precision to the description and understanding of adult language disorders, providing the groundwork for new approaches to the diagnosis and rehabilitation of language disorders. For example, chronometric techniques are now available that permit the millisecond-by-millisecond analysis of auditory language comprehension, highlighting the complexity of the processes required to integrate aspects of word meaning with elements of sentence structure. It now seems clear that at least some adult language disorders involve a disruption in the timing and integration of these processes, which must mean that the knowledge is still there but difficult to access. This discovery has implications for assessment and remediation. Other insights have come from computer simulations that capture some important phenomena in normal language learning and language use. Artificial "lesions" to these models permit the simulation of some aphasic symptoms and provide a means of testing competing theories of language breakdown.

Studies using various forms of functional brain imaging (for example, PET, fMRI and ERP) have shown that different patterns of linguistic input elicit distinct patterns of brain activity. For example, different patterns of regional blood flow are observed in different regions of the visual cortex in response to visual presentation of real words versus unpronounceable strings of letters. Activation studies, as well as behavioral studies of patients with brain lesions, are also providing evidence that language function may not be restricted to the classical language areas of the left cerebral hemisphere. Contrary to early belief that lesions to the right hemisphere have little or no effect on language in most right-handed individuals, recent evidence shows that right-hemisphere injury affects specific aspects of language processing, including prosody and narrative discourse. Other regions of the brain have also been identified in which lesions produce language disorders. These regions include the thalamus, basal ganglia and cerebellum. Activation studies have also documented a relationship of language to these structures. Although the role of these structures in language processing remains to be clarified, the finding that language is related to a wide range of structures has changed the concept of the neural basis for language from one that relates language processing to cortical centers to one in which language processing is related to complex neural systems.

The understanding of language and its biologic bases has also been advanced by the study of impairments in languages other than English. Cross-language comparisons of language disorders have begun to distinguish between symptoms that are universal in their form of presentation and those that are specific to the structure of particular languages. It is now known that deaf individuals who were native users of a signed language can suffer from several different forms of aphasia, and it is also clear that sign-language aphasia is more likely following lesions to the left hemisphere. Because that is also true for spoken language, it may be concluded that the specialization of the left hemisphere for key language functions must involve processes that are not modality-specific.

Significant progress has been made in the assessment and remediation of language disorders. In the area of assessment, new tests are being developed that target specific language capacities and that more adequately reflect the components of the language system as they are presently understood. Computer-assisted assessment and instruction are active areas of research and have begun to reveal previously untapped cognitive capacities in severely impaired individuals. It has been demonstrated that some profoundly aphasic individuals can learn a computerized communication system that involves the manipulation of visual symbols. Explorations in the pharmacologic treatment for language disorders have shown promise for the relief of selective symptoms (for example, impairments of speech initiation may be reduced by administration of bromocriptine, a dopamine agonist). It may be possible to turn these short-term gains into long-term improvement by combining pharmacologic treatment with specific forms of behavioral remediation. Several traditional treatment programs have been shown to be efficacious with specific types of aphasic individuals. They include treatment protocols targeted directly at theoretically defined language components that are found to be impaired. A limited number of these studies have demonstrated measurable improvement among individuals many years after the onset of their language impairments.

Program Goals

The research objectives formulated below reflect the progress that has been made in related fields as well as the opportunities created by recent technologic advances. They are also sensitive to cultural factors that are likely to affect the acquisition of language and its use.

Several general themes are evident across the research areas covered under the Language and Language Impairments section of the National Strategic Research Plan. First, there is a need for further elucidation of normal language function (spoken and signed), both with respect to the process through which language is acquired and the organization, both functional and neural, that underlies its operation in the adult state. Investigations motivated by current theories of language processing in normal subjects employing spoken, written and signed languages will be relevant, together with detailed studies of language breakdown within individuals and clinical groups. Second, there is a need for more comprehensive data with respect to the incidence and prevalence of various types of language impairments in the population. The development of theoretically motivated, methodologically rigorous and culturally unbiased test instruments, as well as the gathering of comprehensive normative data using such instruments, is central to this effort. In light of the diverse racial, ethnic and social composition of society, it is essential that various subpopulations be properly represented in the subject pools for studies of both normal and impaired language processes.

There is also a need to perform comparative studies across different populations to provide information that cannot be obtained from the isolated study of specific groups. These studies should include comparisons across age levels, languages (including monolingual and bilingual speakers), cultural and demographic groups, as well as within and across the different disorders that lead to language impairment in children and adults.

A third theme that is common to the several research areas covered in this report is the concern with brain mechanisms underlying language acquisition and processing, both in normal and abnormal states. There is need to provide a fuller understanding of how language in all of its aspects is related to the anatomy and physiology of the brain. Relevant data will come from lesion studies seeking to map specific language capacities to brain systems and assessments of the functional anatomy of language in normal and brain-injured subjects using current brain imaging techniques. Though other types of research on language stand to benefit from recent technologic advances, it is in the study of brain-language relationships that new technologies are likely to have their greatest impact.

In addition to these general program goals, areas of specific concern can be identified as follows.

In the study of language in deaf and hard-of-hearing individuals, there is need to:

- Pay particular attention to the specific needs of varying types of deaf and hard-of-hearing children acquiring language in different learning environments. The effects on spoken, signed and written language development of early exposure to spoken English, signed English and ASL need to be determined. The effects of differing levels of auditory information on spoken language development need to be rigorously assessed, particularly with regard to improvements provided by new assistive devices. Because hard-of-hearing children's language development has previously received less attention, developmental progress should be assessed separately and monitored.

- Determine the factors that relate to the acquisition of literacy by deaf and hard-of-hearing people, with the goal

of developing methods for enhancing the acquisition of written language by improving English language instruction and by utilizing the child's existing language capacity.

- **Conduct basic research on the structural characteristics of signed languages to enhance comparison with information about spoken languages. In addition, continued investigation of the differences and similarities in the way the brain processes spoken, written and signed languages is needed.**

- **Investigate how signed languages are perceived and learned to provide a sounder basis for the development of methods for teaching signed languages to both deaf and hearing individuals.**

- **Investigate the attitudes of different cultural groups toward individual differences in communication performance and what to do about them.**

In the area of child language, there is need to:

- **Examine the causes of language disorders in children by further investigating the neural and genetic substrates and the impact of early environmental influences on these disorders.**

- **Characterize the linguistic, perceptual, cognitive and motor properties of children's disordered oral, signed and written language as they are manifested across development.**

- **Develop culturally and linguistically sensitive measures of language performance and validate them against external biological, educational and social criteria.**

- **Develop effective remediation strategies based on the most current theories of language, language acquisition and language processing that meet the needs of children from different cultures, socioeconomic classes, language backgrounds and etiologic categories.**

- **Identify those factors that predict persistent language development problems and the consequences of these persistent language problems for later academic, social and vocational outcomes.**

- **Identify the manner in which social systems and cognitive styles differ across cultures and the influences of these differences on language acquisition.**

In the area of adult language, there is need to:

- **Develop new, culturally sensitive assessment tools for the evaluation of specific linguistic and nonlinguistic abilities in language-disordered adults, including methods that provide insights into the time course of language processing and methods that generalize to language and communication in daily life.**

- **Exploit new opportunities for the study of remediation in language-disordered adults from a variety of cultural and** linguistic groups, including studies that take advantage of computer applications, studies that combine pharmacologic treatment and behavioral intervention and studies that provide information about variability in responsiveness to remediation.

- Take advantage of increasingly sensitive neuroimaging techniques to investigate factors that might account for the variations in symptomatology among aphasic patients and of differences in degree and pattern of recovery across patients.

Research Opportunities

Language in Deaf and Hard-of-Hearing People

Research needs for language in deaf and hard-of-hearing people fall into three broad areas: the study of language development in children, literacy in deaf and hard-of-hearing adults, and basic research on sign-language structure and function.

Language Development in Deaf and Hard-of-Hearing Children

There is great variation in the acquisition of spoken and/or signed language by deaf and hard-of-hearing children. Although some children become very proficient, others do not. Overall, there is a need to study the language abilities of deaf children who differ in their communication skills, and the relationship of those abilities to the nature and timing of the learning experiences provided by parents and teachers.

There is some evidence that, if other variables are held constant, deaf children of deaf parents may tend to outperform other deaf children on a variety of academic and psychosocial measures. No full explanation is yet available of this phenomenon, which requires further study.

Studies are needed of normal patterns for the acquisition of ASL and their relation to cognitive and psychosocial development in deaf children of deaf parents. In addition, to understand the normal patterns of such development, it is necessary to pursue parallel studies of disordered courses of development of signed language in the same population.

Since deaf children of deaf parents constitute only about five percent of the population of deaf children, it is imperative to achieve a better understanding of the typical patterns of language development of deaf children of hearing parents.

In addition, because hard-of-hearing children constitute a substantial portion of the population and because even minimal hearing impairment can affect the acquisition of language, it is imperative that a better understanding be developed of the typical patterns of language development of hard-of-hearing children.

Finally, because many deaf and hard-of-hearing children come from African-American, Hispanic-American or other minority group families, special attention should be given to language acquisition in these linguistic and cultural settings. Within this area, then, new studies are needed to:

- Identify and describe how deaf infants communicate nonlinguistically with their parents and how the transition is made from nonlinguistic to linguistic communication.
- Identify and describe the patterns of acquisition of ASL and manually coded English systems for children who are native learners, and also for children who are exposed to ASL and manually coded English systems at a later age and/or from an incomplete source. Studies should include all regional and ethnic dialects of ASL.
- Identify and describe the patterns of language acquisition of children exposed primarily to manually coded English systems.
- Identify and describe the patterns of language acquisition of children exposed primarily to oral language, either alone or in conjunction with Cued Speech. These studies should include particular attention to hard-of-hearing children, whose oral language success and/or problems need further documentation.
- Determine the outcomes of bilingual acquisition by deaf children, for whom ASL is acquired as a first language and English as a second language. It is also necessary to study other combinations of communication systems and the ability to switch among them when appropriate.
- Identify the critical periods for both the natural acquisition of and training in spoken or signed language of deaf and hard-of-hearing children, and describe the effects of delayed exposure to language on linguistic competence and cognitive and academic abilities.
- Identify and describe the invention of gestural language systems by children without formal sign input and the relation of this process to eventual signed or spoken language development.
- Identify and describe the processes of language change that occur when multiple languages are in contact with each other (pidginization) and when languages are acquired from imperfect input (creolization). These reorganizational processes are thought to occur widely in the families and classrooms of deaf children and adults, due to the varieties of English, ASL and other forms of signing used, but are not yet well understood.
- Examine the language environment of deaf and hard-of-hearing children with hearing parents and teachers, and examine its impact on language acquisition, including the quality of the language model provided by the parents and teachers.
- Develop nonbiased assessment materials and procedures to evaluate deaf children in the full range of areas of communicative competence, as well as cognitive nonlinguistic skills. Special care must be taken to ensure that these materials are appropriate for children from a variety of cultural, ethnic and linguistic backgrounds.

- Develop culturally appropriate procedures for identifying and treating deaf and hard-of-hearing children who have language disorders.

- Study the effects of new technology and intervention strategies (such as auditory prostheses, computer-based training systems and holistic teaching methods) and the age at which they are applied for promoting language acquisition by deaf and hard-of-hearing children.

Studies of Literacy in Deaf Children and Adults

Because problems associated with the acquisition of reading and writing skills are among the most pervasive academic and vocational consequences of hearing loss, studies of the acquisition of English literacy must be a primary research objective. The acquisition of English literacy is all the more complicated for deaf learners because English is not acquired naturally by most deaf children. Research should be conducted to:

- Examine the nature of processing words, sentences and texts, with emphasis on successful versus less successful deaf and hard-of-hearing readers, in an attempt to identify the most effective reading strategies. Such studies should include readers from a variety of cultural backgrounds.

- Investigate the relationships among speech processing, sign processing and literacy.

- Examine the interaction of acquisition of signed languages with spoken and written language and begin to characterize the resulting bilingualism. Studies of the order of acquisition of speech and signed languages as it affects children's eventual acquisition of English language and literacy should also be conducted.

- Assess the role of captioning, telecommunication devices, personal computers and other technologic influences and teaching methods in the improvement of the literacy skills of deaf and hard-of-hearing children.

Finally, no widely accepted writing system for ASL exists. However, there is a growing unwritten ASL literature (including stories and poems), akin to oral history in unwritten spoken languages, that can provide a source of knowledge regarding literary forms, conventions and styles for the deaf child. Because this area has not yet been studied, research is needed to:

- Explore the efficacy of teaching ASL literacy to provide a base for the development of English literacy in deaf children.

Basic Research on Sign Language Structure and Function

Although much progress has been made in understanding the structure of ASL, there are still several topics that require extensive research. In addition, further research is needed on comparative sign language analyses. ASL is used primarily within the United States and in some parts of Canada; in other parts of the world, distinct and quite different sign languages are used, for example, British Sign Language, Japanese Sign

Language, etc. This situation presents an opportunity to examine similarities and differences among the sign languages of the world for purposes of theoretical understanding of spoken and signed language universals and understanding how educational sign methods can make the most natural use of the visual-gestural modality. Research is needed to:

- Study further the structure of ASL, particularly its syntax and semantics, including the full range of ASL dialects used by American deaf people from varying regional, ethnic and cultural groups. Included should be studies of the nature of ASL "creolization."
- Study natural signed languages used in deaf communities in other countries, in comparison to ASL, to determine universal principles and dimensions of variations across signed languages.

Further research is also needed on issues of the perception, production, processing and learning of sign language, to reveal the nature of the mental operations entailed in sign language, as compared with those used in spoken language. In particular, research is needed to:

- Investigate the underlying perceptual and motor processes necessary for controlling a signed language, particularly as they may differ from the nonlinguistic processes relevant to spoken language due to the complex nature of space and movement in a signed language. Research is needed in both adults and children.
- Continue to study the processing of ASL, isolating the component operations and their time course, for both native and nonnative signers.

Finally, research is needed to identify and characterize the neural systems that underlie the representation, perception, and production of signed languages, in both adults and children. Major questions concern the degree to which cortical organization is similar or different for spoken and signed languages, and the ways in which cortical organization may be changed by age of acquisition and by early perceptual and linguistic experience. Research is needed to:

- Continue investigation of which brain areas are employed for sign language processing, using event-related brain potential (ERP) techniques as well as newly developing imaging technology, such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET).
- Study how the neural organization of the basic sensory systems and their resulting functioning may be changed by deafness and/or by exposure to sign languages, considering the effects of the age at which these changes occur.
- Characterize more fully the effects of brain injury, and other known causes of language impairment, on sign language comprehension and production. Further careful study of sign-language aphasia in native signers is of particular interest.

Language Impairments in Children

Research needs in the area of language impairments in children are categorized below as falling into five areas: etiology, symptomatology, assessment, intervention and outcome. These directions for research are seen as cutting across all three groups of language disorders in children (SLI, associated developmental disabilities and acquired disorders), although specific needs may be more applicable to one group than another.

Etiology

Scientific and technical advances now provide new and exciting opportunities to understand the bases of developmental language impairments. It is vital that well-developed and empirically supported accounts of the etiologies of child language disorders be developed. These insights are likely to become available through research that will:

- Identify prenatal exposures in combination with environmental experiences that predispose children to language disorders.
- Determine which language disorders are genetically transmitted. Examine the modes of transmission and seek to identify genes, through molecular genetic techniques, associated with language disorders.
- Identify environmental factors associated with language disorders, and document their impact through the developmental period.
- Examine the neural substrates of perceptual, motor, cognitive and linguistic deficits in children with developmental language disorders using new technologies involving neuroimaging techniques, neurochemical methods and animal models.
- Examine the interplay between early learning and environmental experiences, language development and related neural systems.

Symptomatology

Although important advances have been made in detailing the symptomatology of language disorders in children, much of this work has described language characteristics at a single point in time and has not addressed developmental or comparative issues. Considerable work needs to be done on how to differentiate more effectively between language differences from language disorders and how language disorders are manifested within different cultural and linguistic groups. Recommendations for continued work are to:

- Pursue developmental studies of the unique characteristics of the language of children with language impairment and in particular perform comparative studies of these linguistic characteristics across languages, cultures and clinical populations.
- Specify further the contribution of such factors as perception, cognition and motor function to the development and use of linguistic knowledge in children with language disorders.

- **Determine the degree of comorbidity between language disorders and dyslexia, other learning disabilities, attention deficit disorder and psychopathologic disorders.**
- **Develop computer models to test theories of normal and disordered language and reading development.**

Assessment

There have been a number of advances in the assessment of children's language disorders. Considerable work remains to be done in the validation and refinement of existing assessment tools, as well as in the exploration of new methods of assessment to:

- **Establish the validity of diagnostic measures to identify language disorders using a variety of criteria such as etiologic factors, linguistic features and educational progress or social outcome across the developmental period.**
- **Develop assessment tools to identify more accurately language disorders in children of different socioeconomic groups or whose primary language is other than English.**
- **Assess language performance and develop alternatives to normative procedures that will differentiate between language variations and disorders at different ages across socioeconomic, linguistic and cultural groups to identify ways of more appropriately serving these populations.**
- **Develop and study the efficacy of assessment procedures that examine the development of information processing abilities including nonverbal cognitive skills in children with language disorders.**
- **Establish more adequate normative standards for language development among children who develop more than one language or dialect.**

Intervention

Fundamental research on clinical intervention for children with language disorders continues to be needed. This research is both essential and challenging and, in particular, research addressing the following topics is vital to:

- **Develop and test the efficacy of new intervention strategies that apply theoretical models of language acquisition and processing that have been shown to be valid in predicting normal and abnormal language acquisition.**
- **Investigate how etiologic and symptomatic categories interact with remediation strategies across cultural groups (including children living in poverty) to determine how to tailor teaching methods to the specific language learning needs of individual children.**
- **Test the effect of various intervention strategies on children in multilingual environments. These strategies might include teaching exclusively in either the native or second language, teaching**

some language aspects in one language and others in the other, teaching both languages simultaneously and teaching the two languages sequentially.

- Examine the efficacy of augmentative and alternative communicative systems to teach oral and graphic language and to improve the communication skills of persons with severe communication impairment.

Outcome

Due to the developmental nature of children's language disorders, there are numerous consequences that result during the lifetime of individuals with such communication disorders. Current research has begun to provide new insights into these outcomes, but additional attention needs to be given to the following:

- Identify those factors that can be relied upon to predict persistent disorders of language.
- Study the bases for the relationship that has been found between language disorders and psychosocial, behavioral, vocational and academic outcomes.
- Describe the economic and social cost of language disorders.
- Develop valid and reliable outcome measures to determine the efficacy of intervention.

Language Impairments in Adults

Analysis of Processes Underlying Language and Language Impairments

Further research is necessary to characterize the mechanisms that support the comprehension and production of language in normal adults from culturally and linguistically diverse populations. Detailed investigations into the timing, mode of operation and interactions among perceptual, cognitive, motor and linguistic processes are essential to a basic understanding of language and can serve as a point of departure for studies of language impairments. Continued study is needed to:

- Further refine and implement techniques ("on-line" methods) that are sensitive to the structure and time course of normal language processes.
- Develop "on-line" techniques that are appropriate for use with a range of clinical populations.
- Compare and contrast the structure and operation of language processes within the oral, written and signed modalities.
- Describe further the forms of impairment that occur within these modalities.
- Elucidate the relationship between language ability and nonlanguage perceptual, cognitive and motor skills in normal adults.

- Distinguish between deficits that may be specific to the language system from deficits attributable to perceptual, motor or other cognitive disorders and clarify the distinction between them.

- Develop computer models that simulate normal language and its disorders.

Brain-Language Relations

A clearer understanding of the complex relationship between language processing and brain structure and function is required to address a variety of issues relating to language disorders in adults. Studies are needed to delineate further the neural basis of language processing and the neuropathologic determinants of language disorders. Research opportunities exist to:

- Study the neural systems that underlie language processing in normal subjects. This research will require the further development of certain neuroimaging techniques (for example, ERPs, fMRI, MEF and the use of various isotopes with PET) to study the metabolic and physiologic basis of language processing in normal subjects. The success of these efforts will depend as much on the design and interpretation of the cognitive tasks that are used in conjunction with these imaging techniques as on the sensitivity of the imaging methods themselves.

- Use electrocortical stimulation and single-cell recording techniques to investigate brain-language relationships, where such techniques can be applied in appropriate individuals.

- Study variability in the neural systems that underlie normal language use and the determinants of that variability. These determinants may include gender, age, genetic factors, social factors, multilingualism and others.

- Study the nature of the lesions associated with language disorders in adults, including their location, size, etiology and evolution over time. These studies will require quantitative analyses of lesions identified through CT and MRI and exploration of the functional consequences of these lesions using PET, fMRI and ERP.

- Explore the implications of new findings on neural plasticity for the recovery of language functions after brain damage in adults.

Assessment, Intervention and Recovery

There is a close relationship between studies of normal language and clinical approaches to the diagnosis and treatment of language disorders. Remediation is dependent upon assessment (that is, how these disorders are described), and assessment in turn is influenced by the concepts that arise in research on language and its impairments. To achieve a transfer of methodology "from bench to bedside," it is necessary to develop assessment techniques that can be used in clinical settings. These techniques must characterize language disorders in modern terms. It is also necessary to develop therapeutic materials that address these deficits. Specific research opportunities exist to:

- Revise and improve existing assessment procedures to update them to current understanding of the nature of normal language processing and its disorders.
- Develop assessment instruments that are valid for different cultures, linguistic groups, ages, genders and socioeconomic status levels.
- Develop assessment tools that reveal the linguistic and nonlinguistic communicative abilities of language-impaired subjects in natural situations.
- Develop assessment tools that measure the effects of language impairment and its treatment on the quality of life for individuals.
- Investigate the efficacy and efficiency of existing approaches to treatment. Such studies should include assessment of treatment directed toward improvement of language impairments, developing mechanisms to compensate for language impairments and improvement of functional and pragmatic abilities.
- Develop and evaluate computer-assisted instruction as an intervention strategy for language-impaired subjects. These studies should include exploitation of recent advances in computer systems, including interactive compact disc (CD) and CD-ROM (read only memory) technology.
- Develop and evaluate alternative and augmentative communication systems for adults with language deficits.
- Investigate the potential role of pharmacologic treatment as adjuncts to rehabilitative intervention in language disorders.
- Explore methods that can maintain and prolong language function in individuals with progressive degenerative diseases.
- Identify and test the validity of variables that can be used to predict improvement and/or response to treatment.
- Identify the optimum amount, intensity and duration of treatment for acquired language disorders in adults.
- Investigate means, for example computer-assisted methods or the use of volunteers, to provide efficacious treatment at a reduced cost compared to traditional management.

Comparative Studies of Language and Language Impairments

Language disorders can take a variety of forms because the many causes of such disorders affect the system differently and because there are pre-existing differences among the individuals who develop language problems. This diversity of symptoms provides an important research opportunity in that the comparative study of contrasting forms of language impairment can provide information about the nature of the mechanisms responsible for language under normal and pathological conditions. The same facts also pose a significant challenge for clinical practice. The linguistic and cultural diversity of the United States population is increasing; as a result, there is an increasing number of individuals with language disorders that cannot be assessed or treated using standard methods designed for monolingual and monocultural speakers of standard English. New initiatives are needed to:

- Obtain normative data from healthy individuals of various ages to characterize changes throughout the lifespan in patterns of language use.

- Continue comparative analyses of disorders in different languages and dialects on the assumption that language-specific differences in symptoms can help reveal the universal linguistic and cognitive mechanisms that subserve language processing.

- Perform normative studies of language and its disorders in individuals who speak more than one language or dialect. Relevant issues may include the age at and order in which the speaker's languages were acquired, the contexts in which those languages are used, the impact of code switching (that is, mixed use of two or more languages in a single situation) and variations in cognitive style and mode of processing that can be observed in multilingual children and adults.

- Obtain basic epidemiologic information on the incidence and prevalence of and risk factors for language disorders within African-American, Hispanic-American, Asian/Pacific Islander-American, Native-American and other minority group populations, as available data may not be generalizable across these groups.

- Within and across cultural and linguistic groups, assess the impact of socioeconomic status and gender on the incidence and prevalence of language disorders, including recovery and efficacy of treatment, as well as attitudes toward such deficits by relevant cohorts of individuals within these groups.

- Compare and contrast the profiles of language impairment and associated deficits that are observed due to different causes (for example, congenital versus acquired impairments; focal versus diffuse brain injury; specific language disorders versus language impairment in the context of mental retardation and/or progressive dementia).

These challenges can be met only through the collaborative efforts of different disciplines and institutions. This statement is increasingly true for every science, but it is especially important for the study of language and language impairments because languages come in so many varieties and serve so many social, political and cultural functions. For this reason, a high priority should be given to initiatives that bring scientists together around a set of common goals -- to develop new tools, to establish conventions for the use of those tools, to establish patient registries and to build joint archives of behavioral, neurologic and demographic data from disordered populations.

BALANCE AND BALANCE DISORDERS

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Balance and Balance Disorders

Overview: A Current Understanding of Vestibular Function for Balance

Prevalence of Balance Disorders — A Critical Public Health Issue

The vestibular sense organs, located in the inner ear, are critical for control of balance. However, their importance and function are poorly understood by the general public. Perhaps this is because the control of balance is largely an unconscious process. The importance of balance function is typically recognized only after a failure of the vestibular system results in incapacitating problems. Disorders of the vestibular system cause a variety of serious problems, including falls, imbalance, dizziness, spatial disorientation and a blurring of vision. These problems interfere with most activities of everyday life and may prevent employment and limit personal independence.

Although the precise incidence of balance disorders, disequilibrium and dizziness from vestibular disturbance is difficult to determine, it is clear that these disorders constitute a major public health problem. For example, primary disorders of balance and dizziness are often hidden by their acute and serious consequences, such as falls; motor vehicle, boat and airplane accidents; and on-the-job injuries. Falls are experienced by more than 18 percent of persons over the age of 65 and more than 25 percent of individuals over the age of 75. Among individuals who are institutionalized, the incidence of falls nearly doubles. It has been estimated that, among elderly people, up to 50 percent of those who fall and 20 to 25 percent of those who are hospitalized after falling have vestibular disorders. It has been suggested that disequilibrium may be responsible for many of the fractures caused by falling, including 200,000 hip fractures, that occur annually in Americans over the age of 65. Data from the National Institute on Aging (1990) indicates that combined medical and surgical costs for care of individuals with hip fractures exceed $8 billion per year. Furthermore, within this age group, morbidity may be as high as 50 percent and mortality may exceed 35 percent. Vestibular disorders have serious economic and social costs.

Community surveys have demonstrated that, among elderly individuals living at home, over half believe that dizziness prevents them from doing things that they could otherwise do. Overall, it is estimated that 12.5 million Americans over the age of 65 have dizziness that significantly interferes with their life, thereby extracting not only a physical but also a serious psychological toll. For individuals over the age of 65, disequilibrium is one of the two most common diagnoses among short-stay hospital admissions. In fact, the National Ambulatory Medical Care Survey for 1981 found that dizziness was the most common symptom presented to primary care physicians by individuals 75 years of age and older.

Disorders of balance are also common in younger individuals and children. Up to two-thirds of children with acquired deafness have severe vestibular deficits. In most cases their parents and health professionals have not identified their vestibular-related disabilities, often attributing the deficit to motor clumsiness, disorientation or cognitive or emotional limitations. In addition, many individuals who have sustained head injuries have long-lasting balance and dizziness problems related to vestibular system damage.

Although nearly everyone knows someone who has experienced dizziness and/or balance problems, these problems take many forms. The most common type of dizziness is provoked by inclining the head into certain positions, thereby interfering with occupational safety and daily activities. Although dizziness itself can lead to balance problems, disorders of the inner ear can cause severe balance problems even without dizziness. Slow degeneration of the vestibular sensors in the inner ear with aging is associated with postural instability in the dark or on uneven surfaces. Unfortunately, many individuals are not aware that they have an inner ear problem until they sustain a serious injury from a fall.

The psychological impact of vestibular symptoms should not be underestimated. The fear of falling, with the chance of physical injury, adversely affects an individual's sense of independence and affects the quality of life. Similarly, the fear of a sudden attack of dizziness, accompanied by socially embarrassing gait instability (ataxia), nausea and vomiting, can cause individuals to become reclusive. Subconscious fear of movement may play a role in the fear of being in large, open areas (agoraphobia). Subtle dysfunction of the vestibular system may underlie difficulties in learning, writing and reading. Vestibular dysfunction adversely affects an individual's ability to perform the most routine activities, such as taking a shower, performing housekeeping duties or driving an automobile. It may also prevent individuals from holding risk-intensive jobs (for example, telephone lineman, mechanic or bus driver).

With at least half of the people living in the United States being affected by balance or vestibular system impairment sometime during their lives, tremendous health care resources are committed to the medical, surgical and rehabilitative therapy for persons with vestibular disorders. Millions of dollars are spent each year on specific and symptomatic pharmacotherapy for vestibular disorders. The costs of surgical procedures and rehabilitation add many more millions. Advances in basic research, pathology and diagnostic methods have led to more specific medical and surgical treatment. However, the remaining gaps in professional and public knowledge of vestibular disorders and their management result in quality-of-life compromises for those individuals who suffer from vestibular impairment.

In 1976, an estimated $500 million was spent on visits to physicians for dizziness or vertigo. In 1994, the costs for medical care alone are estimated to exceeded $1 billion. To this total must be added the cost of diagnostic testing and treatment. The cost of falls from poor balance, which potentially lead to fractured limbs, hospitalization, surgery, pneumonia and sometimes death, add significantly to this amount.

Balance disorders also exact a military cost. Each year, the Army, Navy and the Air Force lose an average of 30 pilots and their aircraft to accidents caused by pilot disorientation and subsequent error. This loss of material conservatively represents an estimated cost of $300 million per year. In times of armed conflict, this cost increases three to four times. Also, two-thirds of all astronauts experience motion sickness that can severely reduce their effectiveness for the first three days into orbital flight.

A better scientific understanding of balance disorders is needed to identify and treat all of these problems. New research is needed to identify how vestibular pathology causes so many different types of dizziness and balance problems. The current lack of understanding of balance disorders results in misdiagnosis and failed therapy. Individuals with balance disorders see a variety of health care professionals before an accurate diagnosis is made. Some suffering could be partly remedied by improving health provider education on the clinical presentation and management of vestibular disorders.

Although considerable progress has been made over the past decade in understanding balance disorders, research is critically needed: (1) to learn the actual incidence and social effects of balance disorders, (2) to understand how the vestibular organs sense movements, (3) to understand how development, aging, regeneration and genetics affect normal and disordered vestibular function, (4) to characterize normal and disordered balance, gaze and perception of spatial orientation, and (5) to improve the diagnosis and treatment of balance disorders. This research provides the basis for eliminating the excessive, unnecessary suffering, dependence and social and economic costs associated with balance disorders.

Signal Transduction and Transmission

To understand the fundamental basis of balance and balance disorders and to identify and treat individuals with such disorders, further investigations are needed to explain how the vestibular sense organs inform the nervous system about body position and movement.

Signal Transduction

In mammals, there are five vestibular sensors located in each inner ear, adjacent to the structures for hearing. Two of these sensors, the utricular and saccular maculae, transduce linear acceleration forces acting on the head. The other three, the cristae of the semicircular canals, transduce angular or rotational acceleration forces. The five vestibular sensors are contained within the membranous labyrinth, a series of interconnected tubes and sacs filled with a high-potassium fluid called endolymph. The outside of the membranous labyrinth is bathed in perilymph, a fluid low in potassium and high in sodium, like most other extracellular fluids. The components of the labyrinth are so arranged in the temporal bone that they collectively provide the brain with a three-dimensional reconstruction of the position and motion of the head in space.

Each vestibular end-organ contains dark and transitional cells involved in endolymph homeostasis and a sensory epithelium composed of supporting cells and sensory hair cells. Bundles of mechanosensitive stereocilia (hair bundles) protrude from the apical surfaces of hair cells. Gelatinous accessory structures, the otoconial membranes of the maculae and the cupulae of the cristae, are moved by forces associated with active or passive head movements or by certain static head positions (head tilts). Displacement of these structures deflect the hair bundles to which they attach. These mechanical links between head perturbations or displacements and hair-bundle deflection are poorly understood. Deflection of hair bundles opens mechanically sensitive ion channels that allow potassium ions to flow from endolymph into the hair cell to depolarize the cell membrane. The change in membrane voltage modulates currents through other ion channels, located in the basolateral membrane, which modify the receptor potential. Calcium ion influx through channels at presynaptic sites on the hair cell modulates the release of glutamate or possibly other (as yet unknown) chemical transmitters, initiating the neural signal.

Signal Transmission

To transmit sensory information to the central nervous system, vestibular sensory nerve terminals in the labyrinth respond to hair cell transmitters by increasing or decreasing the frequency of nerve impulses from a resting level. These afferent nerve fibers are structurally and physiologically diverse. They innervate one or more hair cells, and afferents innervating different regions of the maculae and cupulae have different response properties. The functional significance of this heterogeneity is currently unclear but is actively being investigated. Vestibular afferents transmit signals to nuclei in the brain stem and cerebellum. At all points in the pathway, resting neural activity is biased upward or downward by positive or negative deflection of the hair bundles or by efferent activity.

Hair cells and sensory afferent terminals receive synapses from cholinergic, efferent fibers that originate in the brain stem. Efferent activity modifies the afferent response and may modulate vestibular responses on a longer time scale.

The afferent vestibular nerves enter the brain stem and contact cells in the vestibular nuclei and cerebellum. Transmission at these contacts involves the release of excitatory neurotransmitter molecules. The receiving cells carry receptors that are highly specialized for the detection of these specific molecules. Excitatory amino acid and gamma amino butyric acid (GABA) receptors have been shown to be present in the vestibular nuclei. However, the molecular subtypes of these receptors, as well as the subtypes of various other neurotransmitter receptors in this region, have not been analyzed in detail. Because these receptors are critical to normal synaptic transmission or activation of intercellular communication, knowledge of their distribution and association with specific vestibular pathways is important for developing specific pharmacotherapy for vestibular disorders.

Development, Aging, Regeneration and Genetics

Normal Development

During embryonic development, the inner ear arises from the otic placode, an invagination of surface and neural ectoderm that closes off to form the otic vesicle. Topological elongations and distortions of the otic vesicle produce the six organs of the inner ear: the three semicircular canals, the saccule and utricle of the vestibular system and the cochlea of the auditory system. Specialized epithelia within each organ produce the mechanosensory hair cells for balance and hearing relatively late in the developmental sequence. The transcription factors and growth factors driving morphogenesis and cellular differentiation are not well understood. Differentiation of epithelial cells into hair cells is apparently inhibited by contact with other hair cells, but the proteins that mediate this interaction are just beginning to be identified.

Aging

Parsing out the causes of balance problems has been difficult, because balance is achieved by a complex interaction of vestibular transduction, joint and touch sensation, vision, multisensory integration in the central nervous system and motor output. Nevertheless, the age-related progressive loss of vestibular hair cells and afferents has been observed in postmortem studies and is known to reach 40 percent by the age of 80. In fact, the extent of afferent loss with aging is greater in the vestibular system than reported in any other sensory system. It is not known why so many individuals lose vestibular function as they age or how to prevent the loss.

Regeneration

Damage to the sensory hair cells caused by ototoxic antibiotics or certain diuretics can cause severe vestibular defects. Although individuals can learn adaptive strategies, the fundamental defect is not curable because human hair cells generally do not regenerate. Hair cells are apparently added to the sensory epithelia of fish, birds and amphibians throughout life, and some hair cell regeneration has been observed in mammalian vestibular organs in culture following ototoxic damage. It is not yet understood how to manipulate chemical factors to promote regeneration.

Genetic Disorders

Some vestibular disorders are caused by defective genes encoding the proteins involved in vestibular transduction and processing; therefore, these disorders can be inherited in families. For example, Ushers syndrome (type I), causing episodic vertigo, is one of the most common syndromic auditory and vestibular disorders. There is a genetic predisposition for developing Meniere's disease, resulting in hearing deficits as well as devastating vertigo and balance disorders in some families, but other inherited vestibular disorders are less well characterized.

Identification of markers for the genes defective in other inherited vestibular deficits will become an important component of diagnosis and treatment. Genetic linkage markers enable prenatal diagnosis to be performed and provide a basis for genetic counseling. They also are the starting point for identification of the defective gene itself. Knowledge of the protein encoded by the defective gene can clarify pathophysiology and help to suggest treatment. Ultimately, methods for gene therapy will be available for treatment of some of these genetic disorders.

Identification of gene defects in mouse mutants, in which experimental manipulation is possible, can aid in identifying human homologues. A number of mouse strains with genetic vestibular disorders have been found, usually having problems with balance or gait. Some of these problems are degenerative disorders that may elucidate the aging process.

Vestibular Functions: Posture, Gaze and Motion Perception

Natural behavior entails a nearly continuous sequence of complex head movements that are registered by the semicircular canals (angular motion sensors) and otolithic organs (linear motion and static tilt sensors); all of these inputs are capable of driving stabilizing movements of the eyes, head and body. These functions are subserved by two classes of central pathways. Vestibular signals drive eye movements through the vestibulo-ocular reflexes and control head and body orientation and movement through the vestibulospinal reflexes. One vestibulospinal reflex is the vestibulocollic reflex, which specifically controls head stability by activating the neck muscles.

Control of Gaze

The vestibulo-ocular reflexes compensate for head movement by generating compensatory eye movements. These compensatory eye movements help maintain binocular fixation on visual targets in the environment and enable a stable image. This reflex operates in response to either passive or active, linear or angular head movements. Because the eyes are automatically driven by head movements, eye and head movements must be closely coordinated during purposeful shifts of the line of sight called gaze. The vestibulo-ocular and vestibulocollic reflexes typically are closely linked and generate complementary results. Together, vestibular influences on eye and head movements are often referred to as gaze control.

Like all vestibular reflexes, those that control gaze are mediated through the vestibular nuclei, with important links to other brain-stem structures, the cerebellum, and higher brain regions. Even at the level of the vestibular nuclei, however, it is clear that vestibular pathways serve to integrate inputs from other sensory modalities (that is, vision and somatosensory), as well as motor-related signals relevant to equilibrium, spatial orientation and control of eye and head movement. Indeed, natural eye/head coordination usually occurs while a person is looking at, or shifting gaze between, objects. The vestibulo-ocular reflex typically operates in conjunction with visual influences on eye movements, part of which share brain-stem neural circuitry closely associated with the vestibular system.

Despite the superficial simplicity of vestibular control of eye motion, three important complexities exist. First, input signals from the semicircular canals and otolithic organs maintain planar and directional properties that must be matched with the pulling directions of the extraocular muscles and muscles of the head and neck if proper compensatory eye and head movements are to be achieved. Second, the effectiveness of ocular responses to head motion, especially linear motion, depends upon the line of sight relative to the direction of motion and the viewing distance. This proper adjustment requires that the vestibulo-ocular reflex be rapidly modulated by nonvestibular signals that convey the current state of the positions of the eyes in the head. Third, vestibular reflexes are under constant, though more gradual, adjustment by virtue of adaptive plastic mechanisms that serve to maintain or restore proper performance despite the physical and neural changes entailed by development, aging and disease. Adaptive modifications in the vestibulo-ocular reflex occur whenever mismatch arises between vestibular inputs and the visual feedback received during compensatory eye movements. These processes have been best characterized for rotational motion and remain largely uncharted or rudimentary for linear motion.

Control of Posture

As a sensor of gravity and head movement, the vestibular system is one of the nervous system's most important tools in controlling posture. It contributes to balance and movement as both a sensory and motor system. As a sensory system, vestibular information combines with visual and somatosensory information to construct an internal representation of the position and movement of the body relative to its environment. As a motor system, vestibular information combines with visual and somatosensory information to control static head and body postures and to coordinate postural movements. Thus, postural stability results from the integration of vestibular signals with other sensory and motor systems to control the forces that maintain equilibrium and appropriate postural alignment.

The particular role played by the vestibular system in any given postural task depends upon the nature of the task and on the environmental conditions. For example, when head stability is critical for good performance or when somatosensory and/or visual information is not available, vestibular information assumes a more dominant role for postural control. Although it was once assumed that the abnormal balance of individuals with vestibular disorders is the simple and necessary consequence of the loss of vestibular reflexes, it is now known that the role of the vestibular system in control of posture is much more complex. This complexity enables some individuals with severe vestibular loss to compensate sufficiently by using other sensory and motor systems to achieve postural stability and coordinated motor function in a certain range of environments and activities. A better understanding of the contribution of the semicircular canals and otolithic system to posture and movement will make it possible to facilitate maximal compensation in individuals with vestibular disorders, and thereby promote maximal functional independence.

Motion Perception

Dysfunction of the vestibular system, particularly the inner ear and its interconnections with the brain, may cause abnormal perception of body movement and position, described by such terms as dizziness, disorientation, vertigo, spinning, floating, rocking, lightheadedness, giddiness, sense of falling, imbalance and unsteadiness or difficulty in walking.

These movement illusions may be accompanied by autonomic (cardiovascular, respiratory and gastrointestinal) dysfunction, resulting in changes in blood pressure and heart rate, as well as the occurrence of nausea and vomiting.

Disorientation (wrongly perceived tilt or motion of the body relative to the environment) is one form of position and movement illusion that can arise from abnormalities in the vestibular system or result from subjecting the normal vestibular system to an artificial environment. Artificial environments include many modes of travel, from highway driving to space flight.

Motion sickness is currently regarded as the brain's response to conflicting sensory messages about the body's orientation and state of motion. The sensors involved include the vestibular part of the inner ear, the eyes and body pressure and joint-position sensors. Nausea, vomiting and associated consequences, including poor concentration, are symptoms provoked by so-called sensory mismatch.

Difficulty in Diagnosis and Treatment

Evaluation of vestibular function has improved in the last 15 years due to the development of tests based on modern anatomic and physiologic concepts and the application of technical advancements. For example, studies of individual neurons are providing data upon which models are being developed to provide a more precise understanding of the vestibular, visual and somatosensory inputs involved in gaze stabilization, balance and orientation.

Technical advancements are making it possible to use angular and linear acceleration devices in clinical testing laboratories for measures of both eye movement responses and postural stability. New video techniques are being developed to record torsional, vertical and horizontal eye movements. New brain-imaging techniques, too, are helping to identify structural lesions in both the peripheral and central aspects of the vestibular system.

In many ways, though, the diagnosis of individuals with vestibular disorders remains primitive and inadequate. Unlike the assessment of hearing or vision, there is no easy way of quantifying the functional status of the vestibular receptors. The need to use reflex motor responses to infer the functional integrity of the labyrinthine sensors complicates the interpretation of what is normal and abnormal. One's sense of the body's orientation and motion in the environment, vestibular perception, is much more difficult to describe quantitatively than are visual or auditory perceptual experiences. Other sensory inputs, especially vision and proprioception, also contribute to balance and spatial orientation, and they must be tested alone and in combination with labyrinthine stimuli.

Furthermore, the relatively crude tests of vestibular function are largely limited to testing the function of the lateral semicircular canals. Usually these are restricted to assessing the contribution to the vestibulo-ocular reflex. Measurements of torsional and vertical eye movements resulting from otolithic organs and vertical canal inputs are not yet clinically available. Quantitative tests of vestibulospinal control of the head stability and balance are not yet possible except for a few sophisticated, research-intensive testing laboratories.

The rudimentary state of vestibular testing means that many individuals with symptoms attributable to vestibular dysfunction from a variety of causes, including trauma, infection, infarction and toxins, are not being properly diagnosed and, consequently, are not being properly treated. Clearly, if knowledge about vestibular disorders, their diagnosis, epidemiology, natural history and response to treatment, is to be increased, better tests of the function of the vestibular system must be developed.

Treatment of vestibular disorders include medical, surgical and behavioral strategies. Behavioral rehabilitation programs that include training in mobility, gait, balance, eye/head coordination and vertigo habituation have demonstrated improvement in balance. This improvement prevents falls and reduces vertigo in elderly persons and others with balance disorders. Specific exercise programs have been shown to facilitate the rate and final level of recovery from vestibular deficits. The use of orthotic/prosthetic devices such as canes and walkers is also beneficial in improving balance and preventing falls. Over 50 medical centers in the United States now offer rehabilitation services to treat vestibular disorders.

Limited understanding of the underlying pathology and neurochemistry of vestibular disorders, combined with the rudimentary state of vestibular testing and the lack of standardized diagnostic criteria, has hampered the development of effective treatment. To relieve suffering from balance and vestibular disorders, better treatment methods must be developed.

Recent Accomplishments

Public Health and Education

The National Multipurpose Research and Training Centers, established by the founding legislation of the National Institute on Deafness and Other Communication Disorders (NIDCD), includes two centers, one in Los Angeles, California and one in Baltimore, Maryland, in which research, research training, continuing professional education and public information dissemination on disorders of balance are major components.

In 1993, the NIDCD and the National Aeronautics and Space Administration (NASA) jointly established a multi-institutional center for vestibular research in Chicago, Illinois and Portland, Oregon. Research supported by the center will delineate the selective role of the vestibular sense organs in balance control and construct models of human postural control based on actual physiologic data.

The NIDCD Clearinghouse provides literature searches, information and identifies organizational resources on hearing and balance disorders (as well as those of smell, taste, voice, speech and language) for health professionals, physicians, industry and the public in conjunction with the Combined Health Information Database (CHID).

The NIDCD National Temporal Bone, Hearing and Balance Pathology Resource Registry, established by NIDCD in 1992, provides a database of the temporal bone and brain tissue specimens representing the pathology of hearing and balance disorders held by 22 collaborating laboratories in the United States. Individual investigators can identify and locate all processed temporal bone and brain specimens in the collaborating laboratories by clinical and pathologic diagnosis. The advent of antigen retrieval and DNA extraction techniques greatly enhance the usefulness of these collections for modern molecular biologic research. Furthermore, it provides a nationwide network to acquire new pathologic specimens. As of June 1994, the Registry contains information on over 10,000 temporal bone and brain tissue specimens. The Registry also sponsors training programs in techniques of the study of the pathology of the inner ear, and in conjunction with the Deafness Research Foundation, it disseminates information on temporal bone research to physicians, scientists and the public.

Signal Transduction and Transmission

Electrophysiological and micromechanical studies of hair cells from a variety of species have provided quantitative descriptions of the transduction mechanism, of mechanical adaptation and of voltage-gated ion channels in hair cells. Some molecular constituents of these processes have been identified, including structural proteins, motile elements and ion channels.

The major ion-transport pathways leading to the secretion of potassium by vestibular dark cells have been determined. Several first and second messengers of ion-transport regulation have been identified. First messengers include extracellular potassium and ATP; second messengers include intracellular cAMP, pH and cell volume.

Biophysical and anatomical studies have revealed that the two types of hair cells, type I and type II, have different potassium ionic currents, have different morphologic features and are innervated differently by specialized afferent terminals. These terminals contain different calcium-binding proteins. Type I and type II hair cells and their afferent terminals are aggregated in different places in the neuroepithelium in some end-organs. These studies also have indicated that type I and type II hair cells are actually heterogeneous populations that differ in ultrastructure and morphology of cilia, depending on epithelial location and afferent innervation.

Morphophysiologic experiments have shown that afferent nerve fibers in a particular end-organ differ in their spontaneous discharge and response properties. This response diversity is related to the branching patterns of the afferents, including their location in the sensory epithelium and the types and number of hair cells that they contact.

Information has been obtained about the response of single vestibular afferent fibers to electrical activation of efferent axons originating in the brain stem. Efferent-fiber stimulation can have a predominantly excitatory effect on afferent activity in mammals and fish, but the effect can be both excitatory and inhibitory in other phyla. Efferent neurons contain classical neurotransmitters such as acetylcholine and a variety of neuropeptides and transmitters (met-enkephalin and calcitonin-gene related peptide) that may influence receptor cells and afferent fibers in the end-organs.

Considerable progress has been made in identifying the neurotransmitters involved in the vestibular system. The excitatory amino acid, glutamate is the primary hair-cell and eighth cranial nerve neurotransmitter. Some primary afferent vestibular processes may also contain neurofilament proteins, calcium-binding proteins, and/or substance P. Neurons of the vestibular nuclei have been shown to contain a variety of different neurotransmitters, some of which coexist in the same cell. GABA and glycine have been suggested as neurotransmitters of several central vestibular pathways. Calcium-binding proteins, which are usually associated with GABAergic cells, may play a role in neurotransmitter release and/or in buffering intracellular calcium to protect these cells from injury. Receptors for acetylcholine and the opioid peptides are also present on central vestibular neurons. This suggests multiple avenues for the excitatory modulation of vestibular cells.

Development, Aging, Regeneration and Genetics

Normal Development

Considerable progress has been made in identifying transcription factors that mediate inner-ear development. Early development of the vestibular organ apparently depends on very specific genetic foci. Retinoic acid receptors and thyroid hormone receptors, which are zinc-finger transcription factors, have been found to be expressed during specific periods of cellular division and differentiation.

There have been qualitative descriptions of the timing of peripheral synapse formation among hair cells, vestibular afferents, and efferents in a small number of mammalian species, including humans. These studies demonstrate (1) an organized pattern of synapse formation concomitant with receptor differentiation, (2) competition by peripheral processes for synaptic sites on hair cells, and (3) the relatively late formation of efferent connections. Studies in avian and amphibian embryos have taken advantage of distinctive central synaptic morphologies to characterize the time course of synaptogenesis by the central axons of vestibular afferents and to test hypotheses about mechanisms of target selection.

Connections of neurons of the vestibular nerve have been found to depend on trophic factors originating in both the inner ear and brain stem. These trophic factors appear to guide and stabilize synaptic connections. Vestibular and auditory end-organs differ in the timing of susceptibility to these trophic factors.

Recent experiments in the microgravity environment of space flight to assess the development of simple organisms and adaptability of vertebrates have shed light on the predetermined and modifiable aspects of development and plasticity of the vestibular system.

Aging

The age-related decline in vestibular sensors and nerves is now known to exceed age-related declines in other sensory systems. Tests of eye movements and postural control in the elderly have identified age-related decline in the ability to adapt both balance and vestibulo-ocular function to changing environments. Deficits, such as cataracts or arthritis, have been shown to unmask vestibular disorders for which there previously was compensation, thereby resulting in a dramatic increase in vestibular symptoms such as postural instability. There is deterioration in postural equilibrium, gaze and spatial orientation. There are also declining adaptive processes that might otherwise restore declining function. These findings have demonstrated progressive disequilibrium with increasing age to be a major health problem that needs further scientific investigation.

Regeneration

Finding methods to regenerate hair cells from stem cells or supporting cells is a major goal for reversing deficits caused by hair cell death. Currently, some regeneration of vestibular hair cells following damage from aminoglycoside has been observed. Trophic factors that stimulate regeneration are being identified. Investigators are still a long way from regenerating hair cells, but there is a concerted effort to do so and great excitement that it may ultimately be possible.

Genetic Disorders

The gene defective in neurofibromatosis (type 2) — an autosomal dominant disease causing bilateral vestibular schwannomas in one of every 40,000 individuals — was recently located on chromosome 22. A novel type of tumor-suppressor gene has been identified and sequenced. Inactivation of this gene may be responsible for spontaneous vestibular schwannomas. If proven, this exciting possibility would have important implications for treatment.

The genes for Ushers syndrome (type I) — causing vestibular deficits along with deafness and blindness — has been mapped to chromosomes 11 and 14. Additionally, families with vestibular deficits as the major disorder have been identified. New genetic methods are accelerating the identification of disease genes in humans. These methods will be applied to preventing vestibular deficits.

Genes are inserted into nondividing cells such as neurons using recently developed techniques for gene therapy . These gene therapy techniques should be applicable to the inner ear. Additionally, gene therapy developed to kill brain tumors is entering clinical trials. Related techniques may be applicable to vestibular schwannomas.

Control of Posture and Balance

Over the last several years, new models of postural control have suggested new research directions regarding the environmentally dependent and task-dependent roles of vestibular function in the control of equilibrium and orientation.

The patterns of muscle activation in the limbs, trunk and neck evoked by natural vestibular stimulation have been described in animal models and in humans, as have the ways they vary with context. There have been studies characterizing the kinematics and kinetics of posture and movement in normal and in vestibular-deficient animals as well as normal and vestibular-deficient humans.

Automatic postural responses have been shown to be sensitive to prior experience, instruction and intention, initial biomechanical conditions, practice, attention and level of anxiety, as well as to the convergence of sensory inputs signaling disequilibrium.

Vestibular information has been shown to be more critical for coordinating complex, multisegmental body movements than simple, quiet stance. The earliest stabilizing responses of the body to destabilization have now been shown to be triggered by somatosensory information, when available, rather than by vestibular information. Although individuals with profound vestibular loss may have normal balance reactions in some conditions, their motor repertoire may be extremely limited.

The effects of vestibular stimulation on posture and balance have been demonstrated to depend on actual somatosensory inputs as well as on perceived illusions of somatosensory state. This suggests a common internal map for the perception of self-motion and automatic postural orientation. The use of somatosensory and visual inputs for postural orientation can be altered as individuals compensate for vestibular disorders. This finding may explain context-dependent instability in some individuals. For example, immediately after a vestibular lesion, individuals may become overly dependent on vision for posture and are likely to fall in confusing, visual environments.

Static and dynamic posturography, which quantifies an individual's ability to balance, can now be used to differentiate types of balance disorders. A new rehabilitative approach to improving balance testing posturography combined with biofeedback is under investigation.

The sense of touch has recently been shown to be as powerful as vision in providing postural stabilization. This discovery has important implications for vestibular rehabilitation and supports the use of a cane to reduce gait instability.

Head stability has been shown to be affected by loss of vestibular function for some tasks and directions but not in others. In individuals with vestibular loss, poor head stability may be the basis for poor motor coordination as well as postural instability.

Postural coordination has been shown to be better in individuals who have experienced vestibular loss during childhood, rather than in adulthood.

Using optimal control theory, scientists have developed robust, computational models of postural biomechanics. These models help differentiate biomechanical from sensorineural constraints on postural motor behavior. They may eventually be able to predict why certain postural movements require otolithic organ and/or semicircular canal information.

There has been further progress in understanding the circuitry that underlies vestibular control of posture and movement, particularly control of head position. Projections from semicircular canal and otolithic organ receptors to a variety of vestibulospinal neurons, as well as otolithic organ-semicircular canal convergence, have been characterized. There is new evidence about the relative role of the vestibulospinal and reticulospinal tracts in head stability and balance control. In contrast to previous concentration on supraspinal pathways, recent experiments with natural stimulation have begun to study the potential contribution of spinal interneurons to vestibulocollic and other vestibulospinal mechanisms.

There has been further investigation of higher level neural control of vestibular reflexes. This work includes modulation of these reflexes by the locus coeruleus, an autonomic region of the brain stem, by the cerebellum and by the motor cerebral cortex.

There has been continued research on the pharmacology and biophysics of neurons in vestibular reflex pathways. Cholinergic pathways to the cerebellum have been identified. In vitro preparations have provided considerable information about pharmacology of neurons in the vestibular nuclei and about their membrane properties.

Control of Gaze

Over the past several years, considerable progress has been made in characterizing the relationships among vestibular inputs, their central processing and integration with other sensory and motor signals, the distribution of these signals to motor-output pathways, adaptive plastic processes that maintain the vestibular reflexes, and the behavior of the vestibular reflexes themselves.

The dynamic and three-dimensional spatial transformations that occur in vestibulo-ocular and vestibulocollic reflexes were described. The patterns of muscle activation that result have also been described, and models have been advanced that successfully predict the muscle patterns that underlie gaze control.

Information has been obtained on vestibulo-ocular reflexes, eye/head coordination and interactions with vision in response to linear acceleration. Eye-movement control has been shown to involve interactions among otolithic organ, visual and contextual (target distance, position and motion) influences. Further understanding of these control mechanisms should yield quantitative clinical tests of otolithic organ function.

Progress has been made in uncovering and characterizing the neural connections that mediate gaze-stabilizing reflexes and in associating the structural and physiological attributes of their neural elements. Efforts have revealed a complexity of interactions among vestibular, visual and proprioceptive inputs relevant to spatial orientation.

The structure and function of vestibulo-ocular relay neurons (that form the middle portion of three-neuron vestibulo-ocular reflex arcs) have been described. These descriptions are in sufficient detail to reveal how convergent labyrinthine inputs to these neurons and their divergent projections to multiple motor pools could contribute to reflex transformations. Neural models that explore these possibilities in a formal way continue to evolve and provide insight into possible roles for neural elements in vestibular pathways.

Identification of the more complex indirect pathways that contribute to gaze reflexes has been fruitful. This investigation has included important regulatory roles of the cerebellum.

Research has begun to define the biophysics and pharmacology of neurons in vestibular reflex pathways. This could lead to new medications to treat vestibular disorders.

Studies of synaptic function are revealing new information on cellular transmission in vestibular pathways. For example, afferents with different response characteristics have been shown to influence and modulate central pathways linked to different reflex functions selectively.

Information is emerging about the higher level cortical control of gaze, and how and where sensory and motor information from multiple sources is combined and processed in specific cortical neuronal structures.

The vestibular and balance control systems have the remarkable ability to maintain useful function in many novel motion environments and to adapt to abnormal function of one or more of their components. Continuing advances in vestibular health care, particularly rehabilitation, rely on progress based upon sound scientific concepts. The significance of central nervous system phenomena associated with the adaptive process (such as modulation of neuropharmacologic sensitivity, reactive synaptogenesis and modification of synaptic transmission), which are thought to play important roles in adaptive control, must be measured. These processes must be correlated systematically with behavior.

In the normal function of the vestibular system, the essential role of adaptive plasticity has been recognized. This system is not static, but is constantly changing in response to changes in the environment or internal elements (for example, inner-ear or central nervous system diseases).

New understanding is emerging about the neural changes that accompany recovery from unilateral labyrinthectomy, including both recalibration of the magnitude of vestibular reflex responses and the balance between vestibular inputs from the two sides (vestibular compensation). Neuronal structures have been identified that participate in compensation and adaptive recalibration. Cellular and molecular alterations underlying these important processes are being explored. Experimental and modeling efforts are applied to identifying potential sites and mechanisms of adaptive plasticity, both in the brain stem and cerebellum.

Perception of Spatial Orientation and Autonomic Control

A critical use of vestibular information is in spatial orientation and motion perception. For many years, vestibular responses were conceived as being automatic reflexes and not subject to conscious control. Recent research has shown, however, that people can use conscious information from vestibular receptors during movement. The information includes the position where they started and information about how far they have moved. Individuals can also use the imagined location of targets to adjust gaze and balance movements. Thus, the cognitive processing of vestibular information is important for perceiving spatial orientation and also for the automatic control of gaze and balance.

Considerable evidence suggests that many brain-stem neurons that regulate the cardiovascular and respiratory systems receive vestibular inputs. Vestibular signals assist in the rapid countering of changes in blood pressure that can occur during unexpected postural changes. A better understanding of the vestibular contribution to these autonomic functions could lead to improved control of the symptoms and signs of motion sickness, including nausea, hyperventilation and pallor.

New computer models of motion sickness suggest that this syndrome is a byproduct of the process of adaptation to conflicting sensory inputs or between expected and actual sensory input. It has been demonstrated that individuals have a remarkable ability to adapt to unusual motion conditions, although this process of adaptation is often associated with motion sickness. When adaptation is finally achieved, the vertigo and/or motion sickness disappears.

Recent studies provide a better understanding of the effects of microgravity on adaptive vestibular function. Research conducted in space flights has shown alterations in perception of spatial orientation as well as in eye movement and postural control. These adaptations occurred during flight and after return to Earth. It appears that the plasticity of vestibular reflexes, for the most part, permits adaptation during the first few days of microgravity. However, there is some concern about the effect of degraded neurovestibular performance after long microgravity exposures. Areas of intense current research include the study of the precise characteristics of adaptive plasticity in this unique environment as well as the aspects of vestibular function involved in readaption to Earth's gravity after long-duration exposure to space. Increased alteration in vestibular control of gaze and postural equilibrium following space flight has begun to clarify the maladaptive consequences of sudden changes in environment.

Diagnosis

Advances in modern technology have made the evaluation of individuals with vestibular disorders a quantitative science. Since the vestibular control of eye movements is the best understood, most direct and most easily quantified vestibular reflex, scientists and clinicians have emphasized eye movements to develop tests of vestibular function. The recording of eye movements in response to vestibular as well as other sensory stimuli is part of the standard vestibular test battery, owing in part to advances in the understanding of ocular motor control in general. These tests have contributed as well to the ability of investigators to locate vestibular lesions and diagnose vestibular disorders. They also help quantify the natural history as well as the response to therapy of individuals with vestibular disorders. The advent of small, but powerful, desktop computers and simple devices for stimulating and recording vestibular responses have made such testing batteries widely available to individuals with vestibular disorders.

Although the caloric test is still the time-honored mainstay of the clinical vestibular testing battery, vestibular diagnosis has been advanced by the use of more natural stimuli. These include self-generated rotations of the head and new mechanical devices that can precisely measure and control the motion of the body. For example, rotational testing is helpful in diagnosing bilateral peripheral vestibular loss in elderly individuals with unexplained disequilibrium. By their very nature, rotational and translational stimuli always stimulate both labyrinths. Recent studies have shown, however, that by positioning the head appropriately and using stimuli that stress the limits of performance of the labyrinth, rotational tests can be used to help diagnose both unilateral and bilateral peripheral vestibular disorders. Galvanic stimulation, which uses a weak electrical current to excite the vestibular nerve in one labyrinth at a time, has recently shown to be better tolerated than previously thought in both experimental animal models as well as in human beings. These new tests are relatively easy to use, take little time and will be valuable in the diagnosis of both vestibulo-ocular and vestibulospinal dysfunction.

More than these advances in technology, however, have improved vestibular testing. Recent physiologic studies have exposed some of the limits of the ability of vestibular sensors to respond to unusual stimuli, for example, those of extremely high speed and acceleration. When vestibular responsivity is asymmetric, as in certain vestibular diseases, these limitations have been exploited to improve bedside diagnosis, both in objective tests (for example, head-shaking nystagmus) and subjective responses (for example, blurred vision). Important new physiologic concepts, such as the central mechanism that improves the low-frequency response of the semicircular canals (so-called, velocity storage), have been applied in the interpretation of clinical testing results. These considerations have helped in the differentiation of peripheral labyrinthine from central vestibular disorders.

In the last few years, knowledge and appreciation of otolithic organ influences on vestibular reflexes have been applied to the evaluation and testing of individuals, in an attempt to meet the long-standing need for a clinical test of otolithic organ function.

Otolithic organs respond to linear acceleration, both the force of gravity and linear motion (translation) of the head. New clinical tests are being developed to test normal and disordered otolithic organ function. Rotation of a subject's head about a vertical or nonvertical axis when the axis of rotation is off-center relative to the labyrinth alters the forces acting on the otolithic organs. The vestibulo-generated eye movements made in response to these modes of rotation are currently being investigated as measures of otolithic organ function. Furthermore, the perception of verticality during rotational motion may provide information on the functional status of the otolithic organs. These represent situations in which linear and angular motion are combined. Measurement of the otolith-ocular reflex in response to pure linear motion has been conducted on parallel swings or in linear sleds. Furthermore, realization of the influence of viewing distance on the otolith-ocular reflex, the direction of the line of sight and the state of convergence of the eyes has led to important conceptual and technical advances in the way that otolith-ocular reflexes should be tested.

The quantitative evaluation of balance also has improved with the use of platforms that compute movement of the individual's center of mass with sensitive force transducers under different conditions of sensory (visual, somatosensory and labyrinthine) inputs. Posturography now includes measures of both static and dynamic balance. Both the orientation of the body to altered visual and surface conditions and the automatic postural responses to surface perturbations lend new insights into the functional basis of balance disorders. This can contribute to assessment of the central and peripheral components of postural instability. Methods are being developed to quantify balance during active movements and reactions to perturbation during movements. Such tests are critical to the evaluation of the effects of physical therapy and to understanding compensation for vestibular disorders.

In the last few years, high-resolution magnetic resonance imaging has been shown to be a useful way to locate lesions in individuals with acute peripheral vestibulopathies. Even the individual sensors of the vestibular labyrinth can be imaged and shown to be spared or involved by a pathological process. A beginning also has been made in more reliably diagnosing inner-ear autoimmune disease by measuring antibody responses to specific ear antigens.

Treatment

Medical Therapy

Following advances made in the diagnosis of specific vestibular disorders, the use of specific pharmacotherapeutic agents for the treatment of peripheral and central disorders continues to evolve. The prevalence of human immunodeficiency virus (HIV) and other immune system disorders has increased and, owing to the improved diagnostic methods available, there has been improved early detection and treatment of these disorders. The role of nutrition, diuretics, vasodilators and aminoglycosides in the management of Meniere's disease continues to be explored. Although little is directly known about the etiology and pathophysiology of neurolabyrinthitis, including vestibular neuronitis, clinicians are forced to continue to treat this spectrum of disorders in an empiric manner. Similarly, with improved diagnostic methods, central vestibular disorders such as vertebrobasilar artery insufficiency, vestibular migraine, familial ataxia syndromes and psychophysiologic dizziness are being treated with specific pharmacotherapeutic agents. Recent improvement in the pharmacologic control of the panic and anxiety disorders often associated with these vestibular disorders is encouraging. These agents are broadly characterized as anticholinergic, antihistaminic, antidopaminergic, tranquilizing and histaminic in nature. Although many of the drugs are helpful in relieving these symptoms, the side effects of drowsiness, altered mental alertness and dry mouth and eyes can adversely affect the lives of individuals in terms of safety (falls, work-related injuries or motor vehicle accidents) and quality of life.

In addition to receiving specific therapy, most individuals with vestibular disorders are currently treated with more broadly acting symptomatic therapy to diminish the sensations of vertigo and dizziness and autonomic dysfunction, such as nausea and vomiting.

Vestibular damage secondary to medication side effects may soon be prevented due to a better understanding of the mechanisms of ototoxicity. It may soon be possible to reduce the ototoxic effect of drugs without altering their therapeutic effects.

The application of cellular and molecular methods has resulted in the identification of probable neurotransmitters and receptors in the peripheral and central regions of the vestibular system. However, a detailed understanding of the neurochemistry subserving vestibular function remains to be completed before specific agonist and antagonist therapeutic agents can be developed. Also needed are further studies of the mechanisms of action of currently used drugs and the distribution of their receptors in the peripheral and central regions of the vestibular system.

Surgical Therapy

Strategies for treating peripheral vestibular disorders surgically include unilateral labyrinthine denervation, selective unilateral elimination of posterior semicircular canal function, repair of perilymph fistulas, endolymphatic sac shunting and vestibular nerve vascular decompression. Improvement in diagnostic capabilities, rehabilitation therapy, intraoperative cranial nerve electrophysiologic monitoring and better diagnostic criteria have decreased the morbidity associated with many surgical procedures. However, the efficacy of many of these procedures remains to be proven. These treatment methods represent a significant financial commitment in the United States. Further research in these areas is needed.

Unilateral labyrinthine denervation may be divided into ablative and nonablative procedures. Ablative procedures include labyrinthectomy (transcanal or transmastoid), which is a short and relatively safe procedure, although all residual hearing is lost. Selective chemical "labyrinthectomy" utilizes the vestibulotoxicity of aminoglycosides to ablate vestibular receptors unilaterally. Intratympanic instillation of gentamicin is a promising method; however, minimizing the complication of cochlear ototoxicity by means of delivery systems or absorption methods remains to be investigated. The instillation of the highly vestibulotoxic agent streptomycin into the labyrinth showed early promise in unilateral vestibular ablation for the treatment of Meniere's disease; however, the results of a recent multicenter prospective study of this method have raised serious questions regarding efficacy. If there is useful hearing in a unilaterally affected ear, selective vestibular neurectomy by means of a middle cranial fossa (MCF) retrolabyrinthine (RL) or posterior fossa (PF) approach is currently the accepted procedure. The MCF approach is technically more difficult; however, advances in the intraoperative monitoring of auditory and facial nerve function may prove to decrease the incidence of facial paralysis and hearing loss associated with this approach.

Selective transection of the posterior ampullary (singular) nerve was developed based on a clear understanding of the pathophysiology of benign paroxysmal positional vertigo and has been successful in more than 90 percent of the small subset of individuals with the disabling chronic form of this disorder. The development of the posterior canal occlusion procedure, which is technically much easier, shows promise for the surgical management of this disorder. In addition, the success of canal-repositioning maneuvers and the application of rehabilitation therapy appears to be reducing the number of individuals requiring surgery.

Recent advances in diagnostic methods such as transtympanic endoscopy and use of perilymphatic protein or dye markers are encouraging as methods for detecting perilymph fistulas. Although these studies have lowered the frequency with which surgical repair of round or oval window fistulas is undertaken, demonstration of surgical efficacy is still necessary.

Another nonablative procedure theoretically designed to correct the pathologic endolymphatic fluid metabolism in Meniere's disease is the shunting of the endolymphatic sac. The efficacy of this once extremely popular procedure was brought into question as a result of a small prospective, double-blinded study performed in Denmark over a decade ago. However, a resurgence in interest in this procedure is currently under way in the United States and Europe. Nevertheless, demonstration of efficacy is still necessary.

Rehabilitative Therapy

The use of specific exercises to reduce vertigo and to improve gaze and postural stability in elderly persons at risk for falling and in individuals with vestibular disorders has become a standard of treatment. Vestibular rehabilitation is focused on (1) facilitating central neural compensation, (2) reducing vertigo with habituation, (3) improving balance, coordinated movement and mobility, (4) improving gaze stabilization, and (5) improving physical conditioning. Therapeutic exercises are based on results of animal research demonstrating that motor experience can increase the rate and extent of recovery following vestibular dysfunction or loss. This research demonstrates that limiting sensorimotor experience can delay and permanently retard recovery. Research to determine the efficacy/effectiveness of vestibular rehabilitation is showing that exercises designed specifically for each individual's functional deficits can be effective in improving balance, reducing vertigo, increasing mobility and speed of locomotion and in reducing head instability. In fact, although both vestibular rehabilitation and vestibular suppressant medication reduce vertigo, balance improves more through the use of exercise. Outcome measures of treatment efficacy/effectiveness now include questionnaires assessing the functional limitations of vertigo, static and dynamic posturography, eye-movement tests and kinematic quantification during locomotion and other activities.

The most significant advance in the rehabilitation of one specific, but common,peripheral vestibular disorder (benign paroxysmal positional vertigo) is the canal-repositioning maneuver. Preliminary experience with this maneuver suggests that it may be effective in relieving the condition, sometimes immediately. The underlying pathophysiologic mechanism is believed to be either a repositioning of displaced otoconia away from the involved posterior semicircular canal or it is a form of central nervous system habituation or suppression of the abnormal vestibular signals.

Despite advances in many areas, significant gaps in understanding the scientific basis of vestibular rehabilitation remain. The physiologic basis for relief of vertigo through positioning exercise needs to be clarified. The usefulness of pre- and postoperative rehabilitation protocols to facilitate compensation and full recovery has not been tested. Functional outcome measures to assess functional limitations and disability are needed. Identification of those diagnoses with the best rehabilitation outcomes is also lacking. The effect of age on improvement or recovery of function needs further delineation, as do the other factors that retard compensation. Finally, new methods need to be developed to habituate to visual motion cues.

Program Goals

Improve Public Health and Education

The true incidence of disorders of balance is difficult to determine. This is because of the lack of diagnostic criteria and gaps in the scientific understanding of the underlying pathology and pathophysiology of these disorders.

A lack of strict diagnostic criteria can lead to vague diagnoses and misunderstanding of the diagnostic tests that are appropriate, as well as the relationship between balance disorders and a multitude of other medical problems. Misunderstandings also relate to the use of prescription drugs. Most health care professionals lack experience in the use of diagnostic strategies and in the treatment of balance disorders, including medication and rehabilitative therapy.

In the general public, there is a poor understanding of the cause of dizziness, of its interaction with a variety of occupational hazards, of the relationship between unsteadiness and medications, and a poor understanding of relatively simple safety and prevention steps that can be taken to reduce the sometimes fatal consequences of chronic disequilibrium.

These factors suggest the following long-term goals:

- Develop diagnostic criteria for clear and more definitive diagnoses of balance disorders, including criteria for the underlying pathologic diagnosis.
- Update epidemiologic evaluation of the prevalence of disorders of balance and their economic impact across the life span and for both genders, based on improved diagnostic criteria.

- Improve the level of diagnostic and therapeutic acumen among health care professionals.
- Develop better methods of assessing the effectiveness of treatment strategies, including drug therapy, surgical intervention and rehabilitative measures.
- Develop a better public education strategy concerning the importance of balance disturbance and its interactions with occupational hazards, medication use and other disease processes and the diagnosis and treatment of these disorders.
- Develop practical means of preventing thel consequence of chronic disequilibrium among the elderly, including the high incidence of falls that occur both at home and in institutions.

Understand Signal Transduction and Transmission

To understand how the vestibular system controls balance, posture and eye movements and regulates locomotion and other volitional movements, it is necessary to understand how the end-organs convert acceleration stimuli to electric signals and how these signals are transmitted to the central nervous system. In addition, understanding the molecular and neurochemical mechanisms of transmission within brain stem and cerebellar nuclei will help define functional circuitry and will lead to improved pharmacotherapeutics. Research is needed to:

- Understand the mechanisms responsible for the production and maintenance of inner-ear fluids and of the accessory structures (cupulae and otoconial membranes) and understand the alteration of these mechanisms in the pathologic state.
- Clarify the mechanical forces acting on the head, cupulae, otoconial membranes and the ciliary bundles of hair cells.
- Uncover the cellular and molecular processes underlying transduction from hair cells to afferent fibers and the modification of these processes by efferent and autonomic pathways.
- Discover the neurotransmitters, neuromodulators, and receptor subtypes in morphologically defined and functionally identified hair cells, neurons and neural circuits.

Understand Development, Aging, Regeneration and Genetics

Understanding the development of the vestibular system is critical for understanding structural and functional relationships in the mature system. Understanding normal development is also critical for recognizing, preventing or correcting developmental defects, whether they arise from environmental or genetic factors. Understanding normal development will help reveal those factors necessary for promoting regeneration of damaged sensory epithelia. Finally, understanding the changes associated with aging will lead to improved diagnosis and treatment of balance disorders. Research is needed to:

- Determine what regulates the pattern of embryonic development that produces the organs of the inner ear, the integrative nuclei of the brain and the synaptic connections among them.

- Identify the factors that stimulate regeneration of hair cells and reconnection to vestibular neurons in order to restore vestibular function.

- Discover genetic defects responsible for inherited vestibular dysfunction and the pathophysiology caused by these defects. Develop techniques for gene therapy to correct genetic defects, to deliver trophic factors to regenerate epithelia or to destroy tumors of the vestibular system.

- Determine the basis for age-related loss of vestibular function and imbalance. Characterize the effects of age on the incidence of and compensation for vestibular pathology.

- Understand the specific functional vestibular deficits that arise with aging and determine to what extent they result from a genetic aging program, infection, trauma or toxic insult.

Characterize Normal/Abnormal Vestibular Function

New concepts of how the nervous system controls balance suggest promising research directions regarding the environmentally dependent and task-dependent roles of vestibular function in control of functional equilibrium, posture and movement in animals and humans. Balance and movement depend critically on how the eyes and head are coordinated to maintain visual stability for gaze during movement. The balance system influences how people feel in general, as well as how their eyes, head, trunk and limbs move. It is important to extend understanding of how sensory signals from vestibular, visual and somatosensory receptors determine the control and perception of body position and movement. Research on posture, gaze and motion perception is needed to:

- Determine the specific role of the individual vestibular end-organs and their integration in control of posture, gaze and spatial orientation. Relate particular vestibular lesions of the semicircular canals and otolithic organs to specific postural, gaze and spatial orientation deficits.

- Understand the specific central integrative functions of neural elements in vestibular pathways. Also understand how multiple sensory, motor and contextual influences are combined, transformed and weighted to produce posture, gaze and perception of spatial orientation.

- Determine, at the behavioral and cellular levels, how compensation and adaptive plastic mechanisms function in states of vestibular dysfunction and altered environments. Define the sensorimotor mechanisms that are important in acquiring these changes.

- Investigate the higher level control of posture, gaze and perception of motion and spatial orientation using

neurophysiological and behavioral approaches.

- **Develop improved animal and mathematical models to elucidate the physiological, behavioral and neurochemical basis of normal and abnormal posture, gaze and spatial orientation.**

Posture and Balance

- **Quantify the behavioral strategies and neural mechanisms used to control balance and postural alignment during active and passive motion in a variety of contexts.**
- **Determine the relative role of the different vestibular end-organs, vision and somatosensation in control of posture and movement. Relate particular vestibular lesions of the semicircular canals and otolithic organs to specific motor deficits.**
- **Characterize interactions between vestibular and other senses as a basis for compensation for vestibular dysfunction and for adaptation to altered environments.**
- **Characterize the neuronal populations that underlie vestibular control of posture. Correlate their biophysical and pharmacological properties with their structure and function.**
- **Discover the way in which the neuronal populations interact to yield normal balance and postural control, using both experimental and computational approaches.**

Gaze

- **Understand the structure and function of neural elements that transform vestibular sensory input to the eye and head movements required to maintain visual fixation on targets in the environment.**
- **Characterize the behavioral strategies and underlying neural mechanisms used to control gaze during active and passive motion, and during combinations of linear and angular motion in three-dimensional space.**
- **Determine the specific role of individual vestibular end-organs and their interactions that drive eye and head movements and the sequelae of selective end-organ lesions.**
- **Determine, at the behavioral and cellular levels, the extent to which compensation and adaptive plastic mechanisms respond to vestibular dysfunction, and define the sensory cues that are important in acquiring these changes. Determine where adaptive changes occur in the brain stem, cerebellum and higher structures.**

Perception of Spatial Orientation and Autonomic Control

- **Determine the role of the individual motion sense organs (for example, semicircular canals, otolithic organs, vision and proprioception) and their integration and adaptation in spatial orientation for healthy individuals in** normal and unusual motion environments.

- Determine the relationships among semicircular canals, otolithic organs and sensory-motor information in spatial orientation of individuals with vestibular disorders.

- Develop improved animal models to investigate the physiological and neurochemical bases of motion sickness.

- Define the specific role that the vestibular system plays in the control of cardiovascular and respiratory function during changes in body position relative to gravity.

- Investigate the neurophysiologic basis of higher level cerebral control of perception of motion and spatial orientation.

Improve Diagnosis

The potential now exists to develop new and improved ways to diagnose and evaluate individuals with vestibular and balance disorders using new tests of labyrinthine function, immunologic methods and brain-imaging techniques. Such techniques can also be used to evaluate the diagnostic criteria, the results of treatment and the objective and subjective functional outcome in individuals with a variety of vestibular and balance disorders, including those attributed to trauma, acquired disease and hereditary and degenerative processes. Research is needed to:

- Develop a reliable, efficient and standardized vestibular testing battery that probes the function of all the labyrinthine sensors and assesses both vestibulo-ocular and vestibulospinal function. These techniques can be used in clinical-pathological correlation using both temporal bones and brain tissues as well as to help evaluate the epidemiologic features, natural history, results of treatment and the objective and subjective functional outcome in various types of vestibular and balance disorders.

- Develop psychophysical tests of perception of spatial orientation and movement in normal subjects and in individuals with disorders.

- Develop tests to evaluate the contribution of neck and other proprioceptive afferents to vestibular function.

- Develop and apply tests of adaptive capabilities and compensatory strategies to predict outcomes and plan therapy in individuals who are to undergo medical, surgical and rehabilitative interventions.

- Develop immunologic, genetic, and brain-imaging techniques for the diagnosis of acquired and hereditary vestibular disorders.

- Acquire temporal bones and brain tissues from normal subjects and individuals with documented vestibular symptoms and signs. Study the tissues with light and electron microscopy and cytochemical methods to enhance the understanding of function and pathologic diagnosis.

Improve Treatment

Understanding the normal neurochemical basis of vestibular function is critical for the development of pharmacotherapeutic agents for individuals with balance disorders. In addition, the efficacy, cost-effectiveness and long-term outcomes of medical, surgical and rehabilitative therapy must be studied and compared.

Improve Medical and Surgical Therapy

- Develop and improve pharmacotherapeutic agents, including agonists and antagonists, for the specific and symptomatic treatment of individuals with balance disorders, motion sickness and vestibular impairment.
- Develop agents and mechanisms for the delivery of these agents into the inner ear for the medical manipulation of diseased vestibular end-organs.
- Determine the efficacy of surgical procedures performed to alter vestibular function using controlled, prospective studies.

Improve Rehabilitative Therapy

- Develop rational vestibular rehabilitation protocols and outcome measures useful for assessing treatment efficacy.
- Determine the effects of training on preventing falls and injury and on improving balance, gaze and motion perception in persons with balance disorders.

Research Opportunities

Public Health and Education

Improvements in diagnosis, treatment and prevention of balance disorders and their consequences require improvements in diagnostic criteria and testing and better understanding of the underlying pathology and pathophysiology of these disorders. Understanding the true prevalence and costs of the disorders depends on the development of these criteria and the education of both the public and health care professionals. Research is needed to:

- Develop clear and clinically useful diagnostic parameters for disorders of vestibular disturbances.
- Study the underlying pathology in human temporal bones and correlate the findings with vestibular disturbances during life to understand better the pathogenesis and pathophysiology of these disorders and to validate diagnostic criteria and treatment strategies.
- Provide epidemiologic data concerning the incidence and prevalence of balance disorders in the population, across the life span in both genders, based on clear diagnostic criteria.
- Evaluate the impact of balance disorders on daily activities and work performance in different age groups.

- Evaluate the association of balance disorders with other disease processes (for example, autoimmune disorders, visual and other sensory disturbances, arthritis, neurogenic and cardiovascular disease, obesity and psychogenic disorders).

- Evaluate the frequency of balance disorders caused by drug therapy for the management of other medical problems (for example, hypertension, diabetes and mental disorders).

- Study and compare the efficacy and cost effectiveness of different medical and surgical approaches to the management of balance disorders.

- Study the efficacy of educational paradigms designed to improve the diagnostic and management acumen of health care professionals, to improve public awareness of the causes, diagnoses, and treatment for balance disorders and the prevention of their consequences (for example, falls, fractures and motor vehicle accidents) and to influence policies for the construction of housing and health care facilities to prevent falls and injuries related to chronic balance disorders.

Signal Transduction and Transmission

To understand the scientific basis for vestibular signal transduction and transmission, immediate research opportunities have been identified in the following areas: fluid production and regulation, mechanical coupling, transduction, receptor potential generation, afferent transmission, efferent control, differences in hair cell and afferent fiber function, gene expression and identification of neurotransmitters and receptors and their patterns of localization. Specifically, research is needed to:

Signal Transduction

- Determine the cellular and molecular mechanisms for active regulation of potassium, calcium and other principal ions in the fluid filling the bony vestibular labyrinth, the endolymph, and within the cells of the vestibular sense organs. Identify the organic constituents of endolymph. Investigate the mechanisms of hormonal regulation of the major ion transporting systems. Describe the mechanisms of bulk-water movement (caused by net secretion or absorption of solutes) across vestibular epithelial cells.

- Describe the motions of the endolymph and the overlying membranes of the vestibular sensory organs, the cupulae and otolithic membranes in response to applied forces associated with head acceleration. Characterize the attachment of the kinocilia and stereocilia to the cupulae and otoconial membranes. Determine the structural and biochemical features of ciliary bundles that shape their responses to applied forces. Measure the movement of hair bundles in response to physiologic stimuli. Determine whether forces generated by hair cells can influence the movement of accessory structures.

- Study molecular components of the transduction apparatus. Identify the proteins that constitute the apparatus, including the mechanically sensitive ion channel, the adaptation motor, the tip link and related connectors. Determine the role of the structural components of the stereocilia and the cuticular plate in transduction. Identify how these structures connect to each other and to the structure of the hair cell.

- Characterize the structural and biophysical properties of hair cells of different types and in different regions of the vestibular sensory tissues. Determine the contribution of hair cell basolateral ionic currents to the modification of the receptor potential and the control of neurotransmitter release. Study the ionic exchangers and the pump proteins in the membranes of hair cells.

Signal Transmission

- Use a combination of biochemical, pharmacological and molecular biological techniques to identify the afferent neurotransmitters released by hair cells and postsynaptic neurotransmitter receptors present in ascending nerve terminals of the ascending neural pathways. Investigate the possible existence of neuromodulators in hair cells and afferent nerve terminals that can modify afferent synaptic transmission. Determine whether there are novel modes of synaptic transmission between type I hair cells and calyx endings.

- Study the locations and characteristics of the ion channels in the afferent nerve terminals that are responsible for the conversion of synaptic depolarization to repetitive spike discharge. Localize the spike-initiation site in the terminal or parent axon using sodium-channel markers. Determine how spatiotemporal patterns of transmitter release, properties of afferent fibers, and efferent activity generate firing patterns of vestibular axons. Develop dynamic models that predict and explain patterns of afferent fiber activity on the basis of the anatomical and biophysical properties of end-organs.

- Characterize the mechanisms of synaptic transmission, including peptide co-transmission, between efferent endings and their postsynaptic targets in hair cells and afferent dendrites. Learn the conditions that modulate the vestibular descending neural activity.

- Identify the transcription factors and immediate early genes that regulate gene expression of receptors and neurotransmitters involved in central and peripheral vestibular neurotransmission. Define alterations in gene transcription that occur as a result of vestibular disease or during compensation and adaptation.

- Employ modern techniques to identify vestibular system neurotransmitters and receptors (for example, in situ hybridization, polymerase chain reaction, subtractive hybridization and immunocytochemistry). These

techniques should be utilized separately and in combination with classic neuroanatomic procedures to elucidate the neurotransmitters or receptors associated with individual vestibular neurons and specific vestibular pathways.

- **Clarify the location and role of glutamate and GABA receptors in the neuronal organization of central vestibular circuits.**

- **Determine the cellular and subcellular localization of the neuropeptides and monoamines. Define their roles in central vestibular neuromodulation.**

Development, Aging, Regeneration and Genetics

A better understanding of neural development of the vestibular system, regeneration of vestibular sensors after loss, and genetic control of the vestibular system promises new breakthroughs in the treatment and prevention of balance disorders common in the elderly. The developing and regenerating system provides insight into the potential for neural plasticity and compensation following injury or age-related vestibular degeneration. New research is needed to:

Development

- **Identify transcription factors and trophic factors that are active at different stages of inner-ear and central vestibular development. Develop animal models, such as transgenic mice or zebrafish, in which factor expression can be manipulated.**

- **Understand the timing of cell maturation in the inner-ear and central vestibular nuclei. Understand how changing biophysical and molecular properties correlate with functional maturation.**

- **Characterize the stages of vestibular synaptogenesis, emphasizing central synapse formation and its timing relative to synaptogenesis in the periphery. Take advantage of species differences in developmental timing to resolve the temporal relations of synaptogenic events. Develop molecular and immune markers for different stages of vestibular synapse formation.**

- **Develop in vitro vestibular end-organ preparations and continuous hair cell lines with which the development of cells can be observed over time. Use these to elucidate the factors regulating cell division and differentiation in the sensory epithelia.**

Aging

- **Determine the extent of functional vestibular loss that accompanies aging in humans. Investigate the relationship of the rate and extent of recovery to the age at the onset of vestibular dysfunction.**

- **Determine the anatomical and biochemical changes of the vestibular system associated with aging, including the quantification of cellular changes in the receptor organs, primary afferents (second-order vestibular nucleus) neurons, and motor efferent elements.**

Regeneration and Genetics

- Develop in vivo models for vestibular sensory end-organ regeneration. These models should further the understanding of synaptic plasticity and the development of treatment strategies for vestibular disorders.
- Investigate the mode of action of suppressor genes that prevent the development of vestibular schwannomas. Determine whether tumor formation can be caused by inactivation of the normal allele of the NF2 suppressor gene.
- Identify human families and new transgenic mouse lines with specific vestibular dysfunction. Locate the defective genes with linkage analysis and identify the genes.
- Investigate familial differences in the vestibular effects of aminoglycoside ototoxicity and identify the underlying genetic differences.
- Develop herpes virus and adenovirus vectors for the delivery of genes into the inner ear and brain stem. Understand which cells can be targets of such vectors. Identify promoters for genes expressed in specific cell populations to increase the specificity of gene targeting. Develop animal models of genetic defects that can be used to test the effectiveness of gene therapy.

Normal/Abnormal Vestibular Function: Posture, Gaze, Locomotion, Other Volitional Movements and Motion Perception

New scientific studies have the potential for understanding the various roles of the vestibular system in posture, gaze, locomotion, other volitional movements and motion perception at both the cellular and subcellular levels as well as at the natural behavioral level. There is now recognition that vestibular function needs to be studied not only in terms of fixed reflexes, but also as an integral part of complex sensory motor behavior. There is a need to understand how the role of vestibular information in posture, gaze, locomotion, other volitional movements and motion perception can change or adapt, depending on context and higher level function such as attention and intent. Some research needs, such as identifying neural elements and mechanisms for adaptation and higher level control, apply equally well to vestibular control of posture, gaze, locomotion, other volitional movements and motion perception, whereas other research needs address issues specific to each vestibular function. New research opportunities in posture, gaze, locomotion, other volitional movements and motion perception are needed to:

- Characterize the structural, biophysical, pharmacological, cytochemical and molecular properties of neurons in different vestibular reflex circuits. Such characterization should be done in animal models and in vitro preparations in which neuron projections are identified to the greatest possible extent.

- Establish the influences of somatosensory, visual and auditory inputs, as well as motor signals on neurons in the vestibular pathways. This should include the influences of sensorimotor context and cognitive variables, such as attention.
- Determine the patterns of convergence of multiple sensorimotor signals in the central vestibular nuclei and the functional associations with other neural circuits and behavior.
- Determine the distribution and organization of otolithic organ and semicircular canal inputs to the vestibular nuclei, cerebellum and related brain-stem targets. Relate these findings to their roles in animal motor behavior.
- Establish the neural sources, targets and characteristics of signals that modulate the vestibular control of eye movements, head stability, balance and spatial perception on a moment-to-moment basis. This would include effects of sensorimotor context, viewing distance and viewing angle.
- Determine behavioral, perceptual and cellular response characteristics during complex combinations of linear and angular motion and interactions with other sensory inputs relevant to spatial orientation, balance and vestibular reflexes.
- Define the role of otolithic organs in the vestibular control of eye, head and body movements during linear and complex (combined angular and linear) motion, especially those produced during (or resembling) natural motor behaviors such as locomotion.
- Extend the development (1) of mathematical models to include experimentally testable models of vestibular pathophysiology as well as normal function and (2) of general models for posture, gaze and motion perception in normal and artificial environments.

Research is also needed to explore the following aspects of adaptation of vestibular function:

- Establish the behavioral characteristics and underlying cellular structures and mechanisms that govern adaptive changes in vestibular pathways. Define the specific sensory cues required for their acquisition.
- Identify the specific sensory signals that trigger and govern adaptive modification of vestibular reflexes and behavior and define their temporal processes. Consider visual and auditory signals relevant to spatial localization and somatosensory cues that supply information about body orientation.
- Determine whether adaptive capabilities can be exploited experimentally to modify the behavioral sequelae of aging and disease.
- Examine the potential relationships between adaptive processes and the

more rapid, context-dependent modifications in vestibular pathways and behaviors.

- Expand the understanding of adaptive plasticity in vestibular reflexes and spatial orientation to include responses to linear and angular acceleration. This should include how signals convey target position, influence vestibular neurons and maintain calibration.

- Examine the cellular and molecular mechanisms that underlie adaptive plasticity and compensation in vestibular reflexes to understand fully the adaptive process. This undertaking requires analysis of alterations in gene expression, transcription, post-translational modification and second messenger systems. This investigation should clarify whether such changes are responsible for alterations observed in adaptive changes.

Explore the relationships between the vestibular system and higher levels of the nervous system, as follows:

- Conduct anatomic and physiologic experiments to determine the pattern of vestibular inputs to the cerebral cortex. Study the integration of vestibular with other inputs in these areas.

- Study modulation and control of vestibular reflexes and behavior by higher centers, including the upper brain stem, cerebellum and cerebral cortex.

- Develop computational models that explore the neural basis of vestibular behaviors and of sensorimotor transformation relating vestibular information and postural coordination. Develop dynamic models of spatial orientation that incorporate consistent and conflicting multisensory inputs and allow for adaption.

Control of Posture and Balance

- Characterize the circuits that link neurons to vestibular motor systems. These studies should emphasize the pathways involved in the vestibular control of neck, axial and limb muscles, including intrinsic and commissural pathways in the vestibular nuclei and spinal interneuron networks involved in vestibular reflexes and behaviors.

- Characterize the sensorimotor strategies, neural mechanisms and adaptive patterns underlying postural control during a wide variety of natural activities and under varying environmental conditions.

- Identify the compensatory strategies used by healthy and vestibular-deficient subjects to adapt to novel sensory and mechanical conditions while preserving equilibrium and postural alignment. Investigate the capacity for sensory substitution to compensate for abnormal or missing vestibular function, to assist in postural stability.

- Identify the role of head stabilization in space for coordination of complex body movements. Identify the role of the vestibular system, and vestibulocollic reflexes in particular, in head stabilization.

Control of Gaze

- Determine the extent of linkage and independence between vestibulo-ocular and vestibulospinal signals in the central vestibular neurons, particularly those involved with eye/head coordination. Identify the nonlabyrinthine influences on these cells.

- Determine the effect of gravitational force on the control of head and neck movement and postural stability.

- Expand the understanding of adaptive plasticity in the vestibular control of gaze during linear and angular (rotational) head movements. Include how signals conveying visual target position influence vestibular neurons and how they maintain calibration.

Perception of Spatial Orientation and Autonomic Control

- Combine measures of spatial orientation and motion perception with physical indices of eye, head and postural movements during tilt and linear acceleration in normal subjects and in individuals with well-diagnosed vestibular disorders.

- Use the free-fall environment of space flight to extend investigations of human spatial orientation and motion perception in the effective absence of gravity.

- Characterize the effects of vestibular signals on individual respiratory muscles, on blood flow to different vascular beds and on the neurons that control cardiovascular and respiratory function.

- Explore the effect of various cerebral cortical lesions on spatial orientation perception in humans and animal models.

- Study the relationships among the perception of orientation, the putative internal model and automatic postural orientation mechanisms.

Diagnosis

Opportunities exist to develop new, improved and cost-effective ways to diagnose and evaluate individuals with vestibular disorders. Such techniques can also be used to evaluate the natural history, diagnostic criteria, results of treatment and objective and subjective functional outcomes in individuals with a variety of types of vestibular and balance disorders, including those attributable to trauma, disease, hereditary and degenerative processes. Research is needed to:

- Develop and evaluate new ways of testing semicircular canal and otolithic organ function, including the use of active versus passive motion. The study of freely moving subjects and the application of galvanic stimulation should employ both postural and ocular motor tests. Build normal and abnormal quantitative vestibular testing databases for valid interinstitutional comparisons.

- Develop tests of the contribution of proprioceptive inputs, including neck receptors, to gaze and balance function.
- Develop portable, ambulatory, noninvasive and telemetric methods of recording and monitoring horizontal, vertical and torsional eye movements, to evaluate individuals with intermittent disturbances of vestibular function.
- Develop improved psychophysical methods for evaluating disorders of perception of the orientation and motion of the head and body, to quantify dizziness and disorientation.
- Develop animal models to establish the reliability, validity and limitations of vestibular tests.
- Develop better laboratory methods to detect immune-mediated and hereditary vestibular disorders. Use brain-imaging techniques for assessing the structural and functional correlates of peripheral and central vestibular disorders.
- Develop tests that exploit central adaptive capabilities and compensatory strategies to predict outcomes in individuals who have vestibular disorders and who are treated with medical, surgical or rehabilitative therapies.
- Employ epidemiological and statistical methods to analyze the results of vestibular function tests in individuals with vestibular disorders. Design questionnaires about subjective symptoms and the ability to perform the activities of daily living. Such studies will help define diagnostic criteria, psychologic and sociologic impacts, natural history, subjective outcomes and objective responses to therapy.
- Determine the pathologic bases of vestibular disorders using studies of the temporal bones of individuals with well-defined clinical histories and examinations and laboratory testing results.

Treatment

A full understanding the normal neurochemical basis of balance and vestibular function is needed for the development of pharmacologic agents that can be used to treat individuals with balance disorders. Also needed is a thorough evaluation of the efficacy, cost-effectiveness and long-term outcomes of surgical, medical and rehabilitative protocols in facilitating compensation, reducing vertigo and improving balance in individuals with vestibular deficits. Regarding various forms of therapy, research is needed to:

Medical Therapy

- Isolate, clone, sequence, characterize and map the genes responsible for peripheral and central neurotransmission in the vestibular pathway.

- Determine the site and mechanism of action of currently used pharmacotherapeutic agents agents for vestibular disturbances and motion sickness.
- Determine the effect of pharmacotherapeutic agents on vestibular adaptation.
- Determine the relationships between balance disorders and psychological dysfunction and the effects of medical treatment on each.
- Improve the efficacy and specificity of intratympanic instillation of gentamicin, including the development of delivery systems and new vestibulotoxic drugs and vectors for the selective chemical ablation of the vestibular end-organs in intractable vestibular disturbances.
- Develop agents active in facilitating vestibular regeneration as well as in selectively destroying diseased vestibular end-organs and the means for their delivery to the inner ear.

Surgical Therapy

- Study the efficacy of surgical procedures for the management of Meniere's disease, including endolymphatic shunt procedures, using prospective, controlled clinical studies.
- Study and compare the efficacy and cost-effectiveness of the medical and surgical management of balance disorders.
- Develop anatomic or electrophysiologic methods to accurately separate the vestibular and cochlear nerves during a vestibular neurectomy.

Rehabilitative Therapy

- Understand the effects of treatment at the pathophysiologic, impairment, functional limitation and disability levels. Develop outcome measures for assessing treatment efficacy, including balance, quality of life, functional independence and prevention of falls.
- Develop new approaches to using biofeedback, novel technologies and sensory substitution strategies to improve function with rehabilitation intervention.
- Quantify functional performance and other changes related to vestibular rehabilitation intervention compared with or combined with medical or surgical intervention.
- Assess the value of treatment using reliable outcome measures that demonstrate changes in balance impairment and function.

VOICE AND VOICE DISORDERS

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Voice and Voice Disorders

Overview

Normal Structure and Function

The voice supports spoken communication and the acoustic representation of language. Speech is the product of adjustments of the larynx and upper aerodigestive tract that act upon and interact with the respiratory airstream to create the physical disturbances that are perceived as speech sounds. Although most people take voice production for granted, reduction or loss of the ability to produce the voice can disrupt or preclude spoken communication, and thus can have far-reaching personal, professional and social consequences. A good voice is important in modern society because there is great demand for effective spoken communication.

The normal voice is produced by using structures in the larynx to rapidly modulate air that is exhaled from the lungs. The larynx acts as a valve between the pharynx (throat) and trachea (windpipe) and, along with other structures in the region, also forms a crossroads between the respiratory and digestive systems. The laryngeal skeleton consists of several cartilages and is suspended in the neck through attachments to the hyoid bone above and trachea below.

The primary laryngeal structures for voice production are the vocal folds (cords). The vocal folds are formed by muscles that are covered with mucous membrane and are moved apart to open the larynx or brought together for closure. The voice is produced by bringing the vocal folds close together and exhaling. When air pressure in the lungs reaches a sufficient level, the vocal folds are blown into vibration, causing the airflow from the lungs to become pulsed. The pulsed airflow is further modified by vocal tract shaping which occurs above the larynx in the hypopharynx, pharynx, nasopharynx, oral cavity and nasal cavities and that affects the quality of the voice during the production of speech. The respiratory system, which is an integral part of the voice production system, provides the energy source and must be coordinated with laryngeal valving and upper aerodigestive tract modulation of the respiratory airflow. Normal voice production is not possible without normal vibration of the vocal folds.

Another important role of the larynx is protection and regulation of the airway. During inspiration, the vocal folds are separated and air passes through the trachea to the lungs. During expiration, movements of the vocal folds participate in the control of the rate of airflow out of the lungs. During swallowing, the larynx is elevated, moved forward and closed tightly, while the tongue and pharyngeal muscles move food or fluid through the oral cavity and pharynx into the esophagus. During a cough, the vocal folds close while expiratory muscles contract to increase pressure in the lungs. The larynx opens abruptly, air rushes out and mucus or foreign material is ejected from the tracheobronchial tree. If the larynx is irritated by particulate matter, reflex closure of the vocal folds and coughing occur. These actions prevent life-threatening aspiration pneumonia.

The same upper aerodigestive tract structures involved in voice and speech production are also required to coordinate the activity of swallowing. Although normal structure and function of the larynx and diseases and disorders of the voice can be studied independently, their interrelations should also be studied. Such integrated studies are critical to improving methods for diagnosis and treatment.

However, there is still a lack of basic information on the structure and function of the laryngopharynx. For example, even now scientists remain unsure of the embryonic origins of parts of the laryngopharynx. As a result, large gaps in knowledge persist regarding innervation of the laryngopharynx, especially sensory innervation.

Information from several domains, such as the neural, muscular, structural, aeromechanical, acoustical and perceptual, will be required to improve the understanding of the complex nature of voice production. This effort will necessitate the involvement of scientists and practitioners from a multitude of disciplines, including basic biological sciences, medicine, physics, engineering, behavioral sciences, communication sciences and the arts. It will also be important to relate such knowledge to specific functions and forms of expression, including those that are psycholinguistic and artistic.

Examples of such disciplines that are of primary importance are molecular biology and genetics. Hundreds of genes have been identified as having a role in normal and abnormal development. Yet, there remains a paucity of information regarding the molecular basis of laryngeal structure and function. Elucidation of the normal development and function of the vocal system at the molecular level is a critical area of research. The application of molecular technology to such studies is essential, and their results will serve as a basis for further studies of the complex cellular and physiologic processes of the vocal system. In particular, these studies will identify genetic factors and distinguish them from environmental effects.

There is also a great need to expand normative database studies to include modifying factors of gender, age and ethnicity.

Diseases and Disorders of the Larynx

Diseases and disorders of the larynx are common, affecting nearly everyone at some time in life. They range in severity from acute laryngitis to airway obstruction and loss of airway protection.

Much of the American workforce depends on good vocal quality to do their work. Consequently, voice disorders can have a substantial negative impact on an individual's productivity and the nation's economy. That impact becomes evident when, for example, a lawyer cannot be heard in court and fails to communicate with the jury, a teacher cannot be heard in the classroom and must cease teaching or a supervisor cannot direct workers at a construction site. Furthermore, for the individual with such a disorder, the social and psychologic effects stemming from inability to be understood are great as is the economic impact.

Most of the activities of the larynx are automatic, and therefore they tend to be taken for granted until there is a disorder that disturbs the normal function. When disease disrupts an individual's vocal or swallowing mechanisms, the consequences can be devastating to the health, well-being and livelihood of the person.

Because of their anatomic location and high-frequency vibration, the vocal folds and larynx have been difficult to examine and study, a fact that delayed research on these important structures in the past. Increased knowledge of the normal functions of the larynx and the availability of new diagnostic tools and new means of analyzing laryngeal function have greatly enhanced scientists' ability to understand the disorders that affect the vocal and swallowing mechanisms. Important progress has been made in diagnosing and treating neoplasms and other lesions of the larynx while preserving function. Less progress has been made toward understanding the molecular basis of laryngeal disorders, especially trauma and scarring. Molecular biological studies of the processes that control wound healing, scar contraction, inflammation and neurogenic abnormalities offer important opportunities for dealing with these problems.

The most prevalent voice disorders result from the way in which the voice is produced. Research is providing new insights into how damage occurs to the vocal mechanism in misuse and abuse of the voice. With that information, early identification and prevention of these voice disorders can be improved. Significant progress has been made in identifying causes of chronic recurring inflammation of the larynx. Important information is being obtained about viral and other infections that cause life-threatening diseases. This work has pointed out important opportunities for further research.

Significant progress has been made in understanding the neural control of the larynx and how it is disturbed by disease. These insights have been translated into more effective treatment for several disorders, such as Parkinson's disease and dystonia. These findings have pointed out important opportunities for research that could lead to great improvements in the treatment of neural abnormalities of phonation and swallowing. Understanding of the growth and control factors that influence the reinnervation of muscles could eventually result in relief for a large number of individuals who suffer from injuries to the laryngeal nerves.

Although progress made so far has been promising, the opportunities for better understanding of the disorders of the vocal system have barely been explored. These opportunities constitute a vital area of research that could lead to improved lives for many individuals.

Application of Technology to Prevention, Diagnosis and Treatment

Advances in technology have led to improvement in the prevention, diagnosis and treatment of disorders of the vocal tract. There has been a steady improvement in technology applicable to molecular and clinical research on disorders that affect voice, swallowing and respiration. Clinicians treating swallowing and voice disorders now have easier access to technologically advanced measurement and analytic computing tools that are useful in the diagnosis and treatment of voice and swallowing disorders. The use of new imaging modalities such as synchronized videostroboscopy, high-speed digital imaging of vocal fold vibration and dynamic magnetic resonance imaging is making it easier to evaluate vocal tract disorders. The widespread use of laryngeal electromyography has led to improved electrodiagnosis of vocal tract abnormalities. Multimodality applications of electrodiagnostic, physiologic and acoustic measurements are now available for the investigation of the normal and abnormal states of voicing and swallowing.

New surgical techniques have been developed to improve the voice and alter voice quality. Restoration of voice after complete loss of voice as a result of cancer or trauma may now be achieved with operations based on the innovative application of technology, including lasers, intralaryngeal framework surgery and new biocompatible implants. The implantation of nerve stimulators and artificial voice devices holds promise as methods for restoring the voice. Work continues on testing the feasibility of laryngeal transplantation in animal models. New voice therapy techniques have been developed to improve rehabilitation of the voice in a variety of disorders, including Parkinson's disease, postsurgical scarring and spasmodic dysphonia.

Augmentative communication and multimedia communication have been improved and offer a better quality of life to individuals with communication impairments . Improvements in speech analysis, synthesis and recognition should further improve technology transfer to industry and lead to clinical applications for people with voice disorders.

There have been advancements in the pharmacotherapeutic and behavioral control regimens for treatment of gastroesophageal reflux laryngitis, a common affliction in professional voice users. The efficacy of systemic and locally injected therapeutic agents has been demonstrated in ameliorating a variety of neurogenic, inflammatory, infectious and aging processes that have a negative impact on the voice. The side effects of common medications on the voice also are being recognized more frequently. In individuals with voice disorders, multidisciplinary evaluation and treatment are usually a more effective approach to delivering voice care.

Recognition of the effects of systemic disease, medication, smoking and environmental toxins on vocal and swallowing function has led to improved efforts at prevention.

The harmful effects of pollution and environmental toxins on vocal health are increasingly being recognized in industrialized urban centers. Similarly, the deleterious effect of smoking on the larynx is well recognized.

Recent Accomplishments

Normal Structure and Function

Anatomy, Cellular and Molecular Biology, and Genetics

Progress is being made in understanding brain function in vocal control through the use of noninvasive techniques such as positron emission tomography and transcranial magnetic stimulation of the cerebral cortex. Both techniques are demonstrating that cortical control over laryngeal muscles is predominantly located in the left hemisphere. In addition, there has been direct electrical stimulation of the cerebral cortex in individuals undergoing neurologic surgery.

Progress has also been made in understanding the innervation of the larynx. One advance has resulted from the introduction of a nerve-tracing technique using Sihler's stain, which renders specimens of non-neural laryngeal tissue transparent while staining the nerve supply. Several novel observations have been made through the use of this technique.

Progress has been made in understanding the structure of human laryngeal muscles. Certain muscles have been found to be composed of several compartments that may have different functions. An important example is the thyroarytenoid muscle. This muscle, in the vocal fold, can be differentiated into two compartments, the muscularis and the vocalis, that may have different functions.

Organotypic cell cultures, composed of both epithelial and mesenchymal cells in a three-dimensional structure, permit near-normal epithelial differentiation. Application of this technique to primary laryngeal epithelial cells has provided insight into the plasticity of the adult human laryngeal epithelium. A single culture of cells can be induced to differentiate along two different pathways, forming either a ciliated columnar or stratified squamous epithelium, as a function of concentrations of retinoic acid in the medium.

The molecular basis for structure and function of cells and tissues is rapidly being defined. Advances in this area include the identification of the role of cell-surface receptors, their ligands, and the subsequent activation of multiple complex signal transduction pathways. The advent of molecular biologic technology has made it possible to study genetic material and identify genetic factors involved in normal development. The Human Genome Project, with its exponential increases in the information in sequence databases, continues to enhance rapidly scientists' ability to identify and clone genes of interest for any tissue. These advances can provide the framework for the definition of the molecular basis of the development and function of the respiratory tract.

Development and Lifespan Alterations

Current knowledge of embryology consists of well-defined descriptions of the stages of laryngeal development in several species, including humans.

Detailed anatomic measurements of the normal larynx have been performed. These studies have shown that the internal structure of the vocal folds is not the same in young children as it is in adults. For example, young children lack a fully developed vocal ligament and have different elastin content in the vocal fold muscle. Current acoustic, aerodynamic and kinematic research is examining the functional consequences of different anatomic structures. Children's physiologic mechanisms for controlling pitch, loudness and vocal quality are different from those of adults. Comparative descriptions have contributed to the study of the structure and function of the human larynx. In particular, ongoing investigations are addressing the neurodevelopment of the larynx.

Critical periods for optimum development of vocal control, as well as periods when a speaker may be at risk for developing dysphonia, have been recognized, but they have not been completely studied. The critical periods that are particularly important for the prevention and treatment of voice disorders include infancy, childhood, puberty and other life-cycle stages characterized by hormonal changes. The onset of a hearing impairment or work in a noisy environment may produce critical periods for the development of voice disorders.

Hormones (growth hormone, androgens and estrogens) affect voice development. Studies have shown that they alter adult pitch; for example, androgen therapy in postmenopausal women lowers the fundamental frequency. Masculinizing neoplasms, male hormone therapy, pregnancy and menopause result in edematous changes in the larynx. Animal studies have shown that androgens alter laryngeal muscle-fiber properties. Molecular biology studies of androgen-regulated laryngeal muscle and cartilage differentiation have shown that two androgen mRNA receptor isoforms are expressed at various stages of the masculine development program in the *Xenopus laevis* model system. These receptors may play a regulatory role in the onset of androgen-mediated myosin expression and cell addition during laryngeal maturation. The effect of androgens on proliferation, survival, synaptic connectivity and function of laryngeal motor neurons is also being studied.

Recent studies have shown that endocrine-type cells in the larynx and trachea express a variety of peptides. Serotonin, calcitonin gene-related peptide and calcitonin appear during development. The significance of these cells is not understood.

Gender Differences

Gender differences in vocal production are currently under investigation. Research has shown that alterations in estrogen and progesterone levels cause cytologic and physiologic changes in the vocal folds. Reinke's edema has been shown to have an increased incidence in postmenopausal women. There is an increased incidence of vocal fold nodules in women. Differences in glottal configuration have been noted between women and men and deserve further investigation. Preliminary work on breathing during speech has resulted in controversy about functional differences between women and men.

Lifestyle and Cultural Influences

Although studies have demonstrated the association of alcohol and tobacco use with cancers of the oropharynx and larynx, relatively little is known about other lifestyle or cultural influences (diet, drug use and exercise) on the function of the laryngeal, respiratory and upper aerodigestive systems. In general, the degree to which these factors lead to deterioration of the structure and function of the pharynx and larynx and vocal quality has not been clearly determined.

Role of Auditory Feedback in the Development and Maintenance of Vocal Control

Individuals with congenital and late-onset hearing impairment display phonation-induced disorders that include voicing errors for consonants, poor voice quality and suprasegmental anomalies of pitch and loudness. Such phonation-related abnormalities have been linked to deficits in the control and coordination of both the laryngeal and respiratory systems. For example, voice-quality aberrations (such as excessive breathiness) in individuals with hearing impairment have been linked to underadduction of the vocal folds, and deviant phrasing has been attributed to air wastage owing to incoordination between the laryngeal and respiratory systems.

Results from recent studies of vocal function in adults and children who are deaf and have received cochlear implants have served to reinforce the importance of auditory feedback in the development and maintenance of vocal control; that is, the acquisition and recovery of vocal control seem to be aided by the auditory feedback provided by cochlear implantation.

Aging

Research has revealed specific anatomical, physiological and biochemical alterations that occur with maturation of the upper aerodigestive system. Laryngeal position and configuration change during development and with aging. Swallowing is also affected by aging. Prolongation of oral transit times and delay in initiating the pharyngeal phase of swallowing have been defined in the elderly. Changes in laryngeal muscle contraction behaviors with maturation also have been reported.

Neurophysiologic studies to examine laryngeal mechanoreceptor (sensory) activity are in progress and will provide better understanding of the neural changes that occur as the larynx ages. In addition, studies of the human superior laryngeal nerves have revealed a large, selective loss of the smallest nerve fibers. This finding may help to explain the age-related dysfunction of laryngeal protection of the airway against aspiration.

A series of histochemical, ultrastructural and stereological studies have been initiated to investigate the aging human larynx and its innervation. Studies of comparative models have demonstrated a number of changes in morphologic parameters that are likely to play key roles in the mechanisms underlying age-related laryngeal dysfunction. Prenatal development of the mouse larynx has been shown to pass through critical stages similar to those in human laryngeal development. Investigations using the murine model make it possible to manipulate the factors thought to have a role in regulating development and aging. In addition, the increasing number of transgenic and knockout mouse lines provides a wealth of possibilities for investigations of the anatomical, cellular and biochemical changes that accompany lifespan changes.

The cellular biology of the upper aerodigestive system also has been found to change with age. Morphological, biochemical and immunohistochemical techniques are being used to examine the distribution of the various types of collagens, other extracellular matrix proteins and basement membrane zone components in the developing and adult larynx.

Muscle Atrophy

It is known that muscle tissue gradually degenerates with age. The main reasons for the degeneration include (1) paralysis of the vasomotor fibers of the sympathetic nerves supplying the muscles, (2) decreased blood supply, (3) decreased levels of mitochondrial enzymes and glycogen and (4) overall reduced metabolic capabilities. This degenerative process involves the age-related death of motoneurons with subsequent reinnervation of denervated muscle fibers by the surviving motoneurons. Since this remodeling can alter the number of muscle fibers innervated by each of the surviving motoneurons, it can contribute to changes in motor control. In addition, the muscle fibers may undergo age-related atrophy, hypertrophy or cell death, which may be specific to the muscle-fiber type.

Deterioration of Joints, Ligaments, Membranes and Other Tissues of the Laryngeal, Pulmonary and Secretory Systems

Vocal deterioration or swallowing disorders may result from restrictions in the movement of the glottal structures, as well as from reductions in lubrication. Specifically, the cricoarytenoid joint, which subserves vocal fold abduction and adduction, can lose its freedom of movement if the capsule of the joint deteriorates. Changes in articular cartilage with thinning and irregularities of the articular surface have been noted with age. Further arthritic changes can result in a joint that is fixed.

Stiffness and lack of elasticity limit the pliability of the aging larynx. This state affects the membranous cover of the vocal fold which results in less motion of the mucosal wave. With vocal stress, the vocal mechanism is less resilient.

Atrophy of mucus-producing glands with aging can lead to changes in the fluid layer of the vocal folds, making normal-quality phonation more difficult.

Biomechanics of the Larynx and Upper Aerodigestive Tract during Vocalization, Respiration and Swallowing

Biomechanics of the Larynx

Biomechanics is concerned with the passive and dynamic characteristics of laryngeal tissues and how these tissues interact to cause motion. The biomechanical problems of the larynx are unique since the vocal folds vibrate. A wide variety of experimental techniques have been applied to the study of vocal fold vibration. Ongoing research is directly or indirectly examining vocal fold vibration in human subjects. Another series of experiments is examining comparative models of vocal fold vibration. Research also is being carried out on excised larynges and on mechanical and theoretical models of vocal fold vibration. All of these studies seek to understand the complex aerodynamics and tissue interactions that produce vocal fold vibration.

Control of Pitch, Loudness and Vocal Quality

Recent investigations have used aerodynamic, acoustic, kinematic, electromyographic, analog and mathematical models to study the control of pitch, loudness and vocal quality. Primary mechanisms for controlling pitch include activity of the intrinsic and extrinsic laryngeal muscles, as well as subglottal pressure. Factors that affect fundamental frequency include vocal fold stiffness (vocal fold tension) and mass. Recently, other factors have been identified that can affect the elastic and stiffness components of the vocal folds: metabolic factors such as nutrients, hydration and temperature, and population factors such as gender and age.

The active and passive forces that contribute to the control of fundamental frequency are also those that serve to alter vocal intensity. In this case, a major force responsible for intensity control is subglottal pressure or the aerodynamic power used to drive the larynx. The control of the aerodynamic power also is regulated by glottal configuration. For example, current research using functional and comparative models has indicated that glottal width is an important variable. Loudness also can be varied by adjusting the supraglottal cavity (pharynx, oral and nasal cavities). Recent research in these areas has focused on the interaction of respiratory, laryngeal and supralaryngeal components for controlling pitch and loudness.

Control of vocal quality is not as clearly defined but is typically described as consisting of various mixes of frequency and intensity components. Examples of terms used to describe vocal quality are "hoarse," "harsh," "breathy," and "register." "Register" has been used to describe different vocal qualities over similar pitch ranges. Terms associated with registers are "pulse" (fry), "modal" (chest) and "loft" (falsetto).

Vocal-Tract Component Interactions

The traditional view of the speech mechanism is that it consists of three systems: the respiratory system, the laryngeal system and the supralaryngeal system. Because of this approach to describing the speech mechanism, investigators historically have tended to treat the three systems as independent functioning mechanisms. More recently though, an emphasis has been placed on studying the interaction of these three systems. The pulmonary and laryngeal components of respiration have a common neural control mechanism so that the vagal-volume response simultaneously regulates thoraco-abdominal and laryngeal muscle functions. Recent aerodynamic studies using both comparative and human models have investigated the simultaneous function of passive forces (subglottal and supraglottal pressures) and active muscular forces (laryngeal muscles) affecting glottal resistance during speech, singing and swallowing.

Swallowing

Swallowing consists of a set of complex muscular actions in the oral, pharyngeal, laryngeal and esophageal regions that are integrated into a functional pattern to prepare and transport food while simultaneously protecting the airway. As such, swallowing is viewed not as one behavior but as a set of coordinated behaviors that vary in their temporal and kinematic characteristics.

The application of electromyography, endoscopy, manometry and combined techniques (such as videofluoroscopy and manometry with computer image analysis) continue to offer new insights and provide more accurate details concerning normal swallowing mechanisms. The physiology of the upper esophageal sphincter has received special attention relative to the mechanisms of opening. The major elements responsible for opening the upper esophageal sphincter have been defined as (1) relaxation of the cricopharyngeal muscle; (2) anterior and vertical laryngeal movement, which opens the sphincter and (3) bolus pressure, which modulates the width of the opening. Recent work has also further specified the influence of bolus variables (for example, volume, viscosity and temperature) on swallowing function. In addition, there have been ongoing efforts to document more fully the nature and extent of normal volitional control over important components of swallowing function, including laryngeal movement, cricopharyngeal opening and airway closure.

Results from recent simultaneous studies of swallowing and respiration have further served to delineate the well-timed pattern between respiratory and swallowing events, including the timing of swallows relative to the respiratory cycle and apneic (breath-holding) interval durations.

Progress continues to be made in efforts to understand the central and peripheral neural control of swallowing. Studies of peripheral control have involved humans and other mammals. Most of the work on central control has been carried out in nonhuman mammals. Recordings from peripheral nerves and muscles and stimulation of peripheral nerves and their receptive fields have provided new information on the sensory receptive fields that evoke or facilitate swallowing. Studies of central control have involved ablation studies, electrical stimulation of and recordings from central neural tissue and the application of pharmacologic agents and immunochemical techniques. These various techniques are serving to provide insights into the general organization of the central swallowing pathway.

Recent studies have begun to examine potential changes that may occur in swallowing function with normal aging. From this work, evidence is emerging that normal aging alters some aspects of swallowing function, including increased oral and pharyngeal transit times, increased magnitudes and durations of pharyngeal pressures and a higher incidence of pharyngeal residue after swallowing.

Comparative and Theoretical Models of Voicing

Comparative Models

Comparative models are an irreplaceable resource for studying the basic processes of voicing. Research is examining the ways in which some species use their vocalizations for social purposes, the basic "grammar" of these vocalizations and how the vocalizations change throughout development. Other investigations seek to understand what aspects of vocalization are lateralized to the left cerebral hemisphere and how they are disrupted by lesions similar to human strokes. Research also is examining how some species learn certain vocalizations. This research is examining what is genetic and what is learned in these vocalizations and how they may reflect a primitive version of human language. Related research is being done on how the brain areas subserving emotion are related to vocalization areas. Ongoing research is investigating the interaction of subcortical structures (periaqueductal gray area) with the nucleus ambiguous in voicing control. This research integrates many different experimental levels: recording, stimulation, neural tracing and ablation of identified cells, and the correlation of these manipulations with vocalization. Other research is studying the mechanism by which subcortical structures (medial geniculate nucleus) distinguish vocalization from other, albeit similar, sounds.

Progress has been made in understanding the sensory physiology of the larynx and pharynx. Recordings have been made from single neurons in the superior laryngeal nerve while changes in pressure and temperature and other variables are applied to isolated regions of the laryngopharynx. Similar research is characterizing the proprioceptive feedback to the brain during phonation.

The structure and biomechanics of the larynx are being studied in a variety of research projects. The intramuscular fluid pressure for different laryngeal muscles is being examined as an indicator of muscle function. This technique may allow small regions of contraction to be measured more accurately and may have advantages over electromyography, in which localization and quantification of muscle contraction can be difficult. Various projects are examining the aerodynamic and mechanical forces in larynges in vitro and in vivo. This line of research seeks to understand the basic mechanisms of vocal fold vibration. Finally, experiments in lower vertebrates are using the vocalization system as a tool for studying basic brain mechanisms such as learning, memory, motor control, and lateralization and genetic, hormonal, and environmental influences on brain structure and function.

Computational Analysis, Modeling and Speech Synthesis

Methods of computer simulation of vocal fold vibration have been effectively used to compare physiologic mechanisms and their control of acoustic signal characteristics. Modern computers make possible the three-dimensional, realistic simulation of vocal activities in real time. A parametric model that characterizes normal voice source signals has been developed and used as a mathematical framework for voice analysis and synthesis.

Exceptional Vocal Behavior

A majority of research on the exceptional voice has dealt with trained singers. There has been an increased use of quantitative methods (that is, objective measures of vocal function, the application of vocal fold and tract modeling and use of voice synthesis) to provide insights into the physical mechanisms that underlie the perception of singing-voice quality, as well as such singing phenomena as the singer's formant and vibrato.

Other studies have sought to compare the vocal capabilities of trained singers with those of nonsingers. Results of this work indicate that trained singers tend to have greater vocal capabilities in the form of larger frequency (pitch) and intensity ranges than nonsingers. In addition, trained singers display higher vocal efficiency than nonsingers, as evidenced by studies showing that singers can produce higher levels of vocal intensity than nonsingers while expending equivalent amounts of aerodynamic energy.

A growing awareness of the special vocal capabilities and behaviors of trained singers has led to recent efforts to include trained singers as special groups in research studies and descriptive databases; that is, to generate separate normative group data for trained singers that can be used in evaluating the voices of individuals who have had singing training.

Advances in the Diagnosis and Treatment of Voice Disorders

Population- and Outcome-Based Research

Existing data indicate that voice disorders affect three to 10 percent of the population in the United States, and an even greater percentage of school-age children and senior citizens. Use of the voice is one of the forms of human communication that is vital for quality of life; loss of the voice is devastating and may be associated with severe depression, stress and withdrawal. The voice also is essential to the functioning of the national economy. Within the working population of the United States, 28 million workers have jobs that require voice use, and 3.8 million have occupations in which voice use is essential for public safety (for example, air traffic controllers, pilots and police).

Data on the incidence of various types of voice and swallowing disorders currently are available primarily from retrospective reviews of selected populations of individuals who have been treated. Extensive data on neoplasms of the vocal tract are available from tumor registries and population databases. Misuse, abuse and overuse (hyperfunction) disorders causing vocal fold nodules, polyps, edema, and dysphonia are prevalent, and they have been cited in numerous studies. Voice and swallowing disorders in association with neurogenic diseases are common; they include Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, stroke and closed head injury. Neoplasms of the vocal tract affect 1,500 children and 50,000 adults annually and result in 5,000 deaths, accounting for two percent of all cancer deaths. Vocal tract neoplasms are associated with tobacco and alcohol use, but the recent identification of potential viral and genetic variables provides new opportunities to explore the interaction of these factors within the population. An apparent increase in death rates among women, African-American and Hispanic-American subpopulations is of concern. Population-based studies that analyze contributing variables remain to be carried out.

Congenital and Acquired Structural Lesions

Congenital and acquired lesions result in serious dysfunction of the vocal, swallowing and breathing mechanisms in thousands of infants, children and adults each year. Such life-threatening disorders include cysts, webs, scarring, lack of normal development and tumors. As the treatment of life-threatening disorders improves, the consequences of interventions (for example, scarring or subglottic stenosis from prolonged intubation) become evident. Important advances have been made in the early detection and diagnosis of congenital and acquired structural lesions of the larynx and pharynx; they include the use of telescopes and fiberoptic technology. The early diagnosis of laryngeal and pharyngeal cancers and other neoplasms is possible in almost all cases if the individual can be evaluated when first experiencing symptoms. Office endoscopy with documentation of the examination has improved the accuracy of diagnosis and follow-up of individuals with neoplasms and other lesions of the larynx without the need for endoscopy under general anesthesia. This improvement has reduced the cost and morbidity of caring for individuals with these disorders. Important progress has been made in developing an understanding of how vocal nodules and polyps develop, and early diagnosis of abnormal phonation patterns offers the possibility of prevention of vocal nodules and polyps.

Major advances have been made in the treatment of non-neoplastic congenital and acquired structural lesions such as subglottic stenosis. New approaches to laryngotracheal reconstruction have greatly improved the mortality rate in children affected with this disorder. New laser technology is available for treating subglottic hemangiomas in infants and papillomas in children and adults.

Laryngeal and respiratory tract papillomas are benign neoplasms in children and adults that are caused by human papilloma virus infection. These neoplasms may rapidly obstruct the airway. Prevention of death from suffocation often requires repeated surgical removal of the papillomas, sometimes every few weeks. The scarring from repeated surgical procedures frequently results in permanent voice damage, even though the neoplasms are controlled. Recent advances in the understanding of recurrent respiratory papillomatosis should eventually improve management of this disease. Abnormal response to growth factors appears to be important in papilloma proliferation and contributes to the failure to differentiate into normal tissue. Genetic susceptibility to development of neoplasms after papillomavirus infection also has been identified. Several clinical trials are currently under way to evaluate alternative or adjunctive therapies for respiratory papillomatosis. These experimental approaches include the use of interferon, ribavirin and photodynamic therapy with new photosensitizers.

Numerous recent studies have explored the possible role of human viruses in the development of head and neck cancers. Epstein-Barr virus is associated with nasopharyngeal cancers. It appears that the human papillomaviruses are present in perhaps 30 percent of neoplasms of the vocal tract, and that these viruses may play a significant role in cancers of the tonsils, base of the tongue and adenoids. In contrast, human papillomaviruses appear to be present in only two to five percent of other head and neck cancers. Therefore, even among mucosal squamous cell carcinomas there are probably differences in the specific mechanisms of malignant transformation. Important questions about the mechanisms of specific tissue susceptibility to viruses and other carcinogens demonstrate the need to study the role of environmental and genetic cofactors in the etiology of specific types of head and neck cancers.

Important and constant progress has been made in the early detection of cancers of the larynx and pharynx. Genetic markers for several different types of malignancies have been identified, and these markers can now be detected in cells from the respiratory tract by using molecular biology methods. This new finding provides the potential for very early detection of preneoplastic and neoplastic lesions and potentially can be used to monitor the progression and recurrence of cancer. Progress has been made in the identification of specific proteins that are expressed in cancers, and may provide opportunities for screening tests for early identification and new targets for therapy.

There have been important advances in treatment for individuals with precancers and early cancers. The efficacy of conservation surgery has been demonstrated, and reconstruction has been refined to improve the options available in individuals with cancer of the vocal tract. Treatment of laryngeal cancers with combination chemotherapy and radiation therapy has shown promising results in sparing the functions of the larynx without compromising survival. Retinoids may have promise in the chemoprevention of cancers in individuals at increased risk for vocal tract cancers. Photodynamic therapy is being tested as a treatment for superficial malignancies of the pharynx and larynx. Important progress has been made in the ability to diagnose and treat swallowing dysfunction after treatment of vocal tract cancers, and research on evaluation of the swallowing function has been translated into the training of therapists who can be effective in the rehabilitation of individuals with swallowing dysfunction. Important progress has also been achieved in the development of prostheses for the production of speech in individuals who have undergone laryngectomy.

Some scientists believe there is a relationship between chronic or recurrent irritation and development of epithelial tumors. Gastroesophageal reflux - or more accurately, gastropharyngeal reflux - is now recognized as commonly associated with chronic laryngeal problems and recurring inflammation. Signs of gastropharyngeal reflux include chronic sore throat and dryness, hoarseness, chronic cough, chronic throat clearing, and contact ulcers. An entirely new understanding has emerged of the role of gastropharyngeal reflux of stomach acid in causing inflammatory disease of the larynx. This finding has resulted from investigators having a greatly enhanced ability to view the posterior larynx and glottic wall and to appreciate color differences. The use of magnifying telescopes with superior light-carrying fiber optics has led to greatly improved recognition of posterior chronic laryngitis as a very common disorder. This has enhanced the ability of clinicians to prevent inflammation in individuals who are at higher risk of complications during and after surgical procedures.

New phonosurgical procedures have been developed to treat voice disorders caused by paralysis, aging and scarring. Phonosurgery is a new surgical discipline specifically designed to improve the voice. Helped by better assessment techniques and better understanding of pathophysiology of voice production, new phonosurgery may be anticipated.

One of the major problems in treating individuals who have had laryngeal disease is dealing with glottic insufficiency. There are now a number of new phonosurgical procedures available to augment the position and shape of the vocal folds to improve the control of airflow and quality of voice in individuals who have experienced damage to the larynx or its nerve supply. Advances have been made in the application of objective measurements developed through basic voice research to the evaluation of the efficacy of these techniques. There has been important growth in the amount of research on the ways in which diseases and disorders of the larynx affect voice and other important functions of the larynx.

Trauma

Progress has been achieved in the reconstruction of tracheal defects, but there remains a need for more research on better treatment of the life-threatening problems in the airway that can result from trauma.

Although important research has been undertaken to improve methods of dealing with scarring of the larynx after injury or surgical treatment, more work needs to be done. There have not been major changes in clinicians' ability to treat trauma of the vocal tract, and there are great opportunities for research in this key area.

Neural Lesions and Disorders

Neural-based laryngeal problems account for a substantial portion of all voice and swallowing disorders. Voice and swallowing disorders may be the first sign of a neurogenic disease, including peripheral disorders such as laryngeal paralysis or central disorders such as Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, dystonia, closed head injury and stroke. Symptoms of neural voice disorders may range from a mild reduction in vocal quality to a severe reduction in speech intelligibility.

Major improvements have been achieved in ways to evaluate and diagnose neural disorders of the larynx. Being able to view and record the movements of the larynx has improved investigators' understanding of how particular neural disorders affect laryngeal functions. Acoustic, glottographic, aerodynamic and electromyographic techniques have emerging roles in the documentation and diagnosis of neural laryngeal disorders. Progress has been made in the treatment of some neural disorders of the larynx, such as Parkinson's disease and focal laryngeal dystonia.

Peripheral Disorders

Injuries to the laryngeal nerves affect the larynx and upper aerodigestive tract. Injuries to the recurrent laryngeal nerve results in paralysis of the vocal fold. The most frequent causes of the injury are operations of the skull base, neck and chest. Tumors, radiation treatment or infections along the path of the vagus nerve also can affect laryngeal function, producing alterations of phonation, airway protection and respiration. Unilateral laryngeal paralysis can result in hoarseness and aspiration owing to incomplete closure of the vocal folds. Compensatory behavior may include hyperadduction of the mobile vocal fold and associated structures. Bilateral paralysis is potentially life threatening because the airway may be compromised. Vocal fold paresis or paralysis also may accompany peripheral neuromuscular disorders such as myotonic muscular dystrophy and myasthenia gravis.

Central Disorders

Laryngeal dysfunction accompanying disorders of the central nervous system is now being studied in relation to problems with vocal fold closure and steadiness. Parkinson's disease, closed head injury and multiple sclerosis are examples of neurologic disorders that may result in limited vocal fold closure (hypoadduction) and reduced vocal loudness. Dystonia and Huntington's disease are examples of neurologic disorders that may result in increased vocal fold closure (hyperadduction) and tight "pressed" voice. Vocal unsteadiness includes tremor, voice breaks or hoarseness. Vocal tremor accompanies a number of neural disorders including essential tremor, Parkinson's disease and cerebellar disorders. The voice disorders accompanying these diseases may severely reduce the individual's ability to communicate. The swallowing disorders associated with these diseases may significantly limit the individual's oral intake of nutrients.

Systemic Disorders Affecting the Larynx and Upper Aerodigestive Tract

Systemic disorders can alter the function of the vocal system. They include effects of pharmacotherapeutic agents for unrelated diseases, hormone fluctuations and imbalances, connective tissue diseases and genetically determined keratin disorders. A key advance has been the growing awareness that these factors have a profound effect on voice production and swallowing. Hormone receptors have been identified on laryngeal epithelium, and the tissues clearly respond to hormone changes associated with endocrine disorders, hormonal therapy for diseases and age-related changes. The impact of connective tissue disorders, including arthritis, lupus and sarcoidosis, has been recognized, but more research is needed to define mechanisms and management of these diseases. The continuously increasing use of drugs for nonvoice disorders will have increasing effects on the vocal system. These effects need to be considered in drug evaluations and usage. Diseases of keratin structure and function, generally considered as skin diseases, also impact the epithelium of the larynx. Transgenic mice that mimic these keratin disorders have recently been developed. They will be useful in studying the effects of expression of specific keratin gene mutations on vocal tract epithelia.

Psychogenic Disorders of the Larynx and Upper Aerodigestive Tract

Psychogenic disorders of the larynx and upper aerodigestive tract are encountered occasionally in the clinical setting. However, because they are often not well understood etiologically, accurate incidence data are not available. It is estimated that the incidence may be from 4.4 percent to more than 30 percent, depending upon ages included in a given survey and definitions utilized. For example, hyperfunctional vocal fold behaviors and laryngeal disorders resulting from vocal abuse may be clustered with a psychologic disorder such as a conversion reaction. It should be noted that data on the incidence of various psychogenic voice disorders are primarily available from retrospective reviews of clinical cases.

Psychogenic disorders may be primary disorders or may be secondary to a loss of communication skills. Disorders of a psychogenic nature include aberrant breath control, pitch, loudness and quality of the voice, as well as muscle tension dysfunction, vocal fold hypofunction and paradoxical vocal fold adduction. It is often difficult to distinguish voice symptoms caused by a psychogenic problem from those evidenced by an idiopathic organic disorder. For example, a conversion aphonia is the manipulation of psychologic stress into a physical manifestation - in this case, no voice.

Misuse and Abuse Disorders

Disorders of misuse, abuse and overuse and are the most prevalent and preventable of the voice disorders. They represent a reported 25 percent of adult disorders in otolaryngology practice and 36 percent of children treated for speech disorders. Vocal misuse or abuse implies a mode of vocal production that places undue strain or stress on the structures participating in the production of the voice. The result may be frank changes or damage to the tissues of the vocal folds and related structures, resulting in dysphonia.

Vocal misuse implies inappropriate breath-control pattern, pitch, loudness or quality inappropriate for the individual's laryngeal mechanism, placing strain on the system. Vocal abuse is typified by loud vocalization, throat clearing, chronic coughing or excessive vocalization without periods of vocal rest. Overuse is the ongoing use of the voice for long periods of time with insufficient rest or the use of the voice over a shorter time in abusive ways. Risk factors include loud talking in a noisy, smoke-filled or dry atmosphere, chronic coughing, throat clearing and use of an inappropriate habitual speaking posture. Many forms of vocal abuse are associated with disease processes such as upper respiratory infection, asthma and gastroesophageal reflux that may increase the tendency to cough. Some medications prescribed for asthma, for example, may actually contribute to reduced efficiency of the vibrating structure. This condition may lead to chronic abuse or increased tension in vocalization and subsequent vocal fold irritation or swelling. These vocal behaviors cause a variety of lesions, including vocal nodules, polyps, hemorrhage, polypoid degeneration, chronic edema and vocal fatigue. Further, toxic environmental elements in the workplace have been shown to contribute to allergy and upper respiratory disease that, in turn, may lead to chronic cough and vocal fold irritation. Studies that lead to a better understanding of the anatomy and physiology of the vocal mechanism have been useful in furthering knowledge of this category of voice disorders. For example, histologic studies of the larynx, defining the ultrastructure of the vocal fold in injury, suggest that vocal nodules are the result of damage to basement membrane zone structures.

Influencing Variables

Multicultural Issues

Much of what is known about vocal diversity and pathology across races or cultures is based upon clinical observations, anecdotal evidence and doctoral dissertations. Therefore, our current responses to even the most basic queries in this area of communication disorders are limited to pitch and its physical correlate, fundamental frequency, which appears to have garnered most of the research focus, and to clinical data on disorders associated with specific lesions. It is likely that non-Caucasian and non-European individuals participated in surveys and large-scale studies of voice disorders. However, the pertinence of cultural identity and ethnicity, including religious values and observances, nutrition, attitude toward medicine and illness was not noted or reported.

Hoarseness continues to be the predominant dysphonia in children up to age 18, with vocal nodules being the most frequent cause of hoarseness. Evidence suggests that African-American youngsters from economically depressed inner cities exhibit more than twice the incidence of hoarseness than do Caucasian children in other communities, and Hispanic-American teenagers from southern California have more than twice the incidence of dysphonia as Caucasian adolescents in the same or similar communities. The oncology literature offers an uneven distribution of laryngeal carcinoma across race.

The Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI) has gathered current and comprehensive data on United States incidence and survival statistics since 1973 in nine regions or registries (Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco, Seattle and Utah). It contains an analysis of Caucasian, African-American, Native-American and Asian/Pacific Islander-American populations for a multitude of cancer sites. SEER findings indicate that the African-American population has an incidence rate for laryngeal cancer 50 percent higher than the Caucasian population, with the higher incidence spanning all age categories above 25 years. There is an even higher incidence for Hispanic Americans over age 65, and a relatively low incidence of laryngeal cancer in Native Americans.

These SEER findings may have cultural implications as well. Choices of diet and lifestyle factors, attitude toward illness, and the use of medical practitioners and medicines are culturally based, and adequate medical services may be limited in large portions of non-Caucasian and non-European ethnic populations of American society. Ethnic rather than racial analysis might provide more valuable insight into risk factors in culturally diverse populations in the United States.

Gender

Male and female voices differ acoustically and perceptually, and there are clear gender differences in laryngeal and respiratory anatomy and physiology. Hormonal, metabolic and genetic factors differ by gender. Menstruation and pregnancy cause changes in fluid retention in the vocal folds and in the degree of dryness of the mucosal lining of the respiratory tract. Vocal fold edema and increased risk of hemorrhage have also been observed during menses. Women seek treatment with greater frequency than men for many voice disorders, including vocal nodules, spasmodic dysphonia, Reinke's edema and changes in pitch range and quality. On the other hand, contact granuloma and contact ulcers are more often observed in men.

Psychosocial and cultural factors that affect men and women differently also affect vocal health. They include diet and other aspects of lifestyle, use of medication, willingness to seek treatment and choice of occupation. Bulimia, which is predominantly a disease of young women, may damage the mucosal lining of the larynx. Occupations typically associated with women, such as teaching and aerobics instruction, appear to involve increased vocal stress, and men in sales tend to exhibit a higher incidence of benign vocal fold lesions than men in other careers. Society places vocal role expectations on both genders that can result in inappropriate pitch, loudness, vocal quality and breathing patterns.

Aging

People over the age of 65 years represent a growing and changing segment of American society. Increased longevity and activity increase the demand for an enduring voice. Age-related changes in the larynx include loss of elasticity and muscle tone, calcification of laryngeal cartilages and increased dryness of the mucosal lining. The most frequently observed vocal pathophysiology during these years is bowing of the vocal folds, although several neurogenically based conditions, including secondary voice problems, may also occur at this time. In addition, senior citizens may exhibit benign mucosal lesions of the vocal folds, as well as vocal fold swelling and hyperfunctional vocal fold activity owing to occupation and personality. Studies have shown that the voice of the elderly is characterized by a decrease in pitch in women and a slight increase in men. Reduction in loudness and altered vocal quality often occur. Although these changes may not be abnormal, voice therapy is sometimes sought to minimalize them.

Environment

Environmental factors are thought to cause or perpetuate voice disorders. Noise, air pollution (including gases, fumes and smoke) and relative humidity are factors that singularly or in combination may cause or maintain a particular disorder. Allergic reactions causing vocal disorders, which may be aggravated by ongoing environmental changes, are being reported with greater frequency.

Lifestyle

There is growing awareness of the effects of lifestyle including diet, smoking, rest and sleep, drug use, exercise and alcohol consumption on the functions of the larynx and upper aerodigestive tract. Gastroesophageal reflux causing throat and voice complaints can be controlled by changes in lifestyle and eating habits. This correlation implies a critical need for outcome research in voice disorder prevention, diagnosis and treatment.

Application of Technology to Prevention, Diagnosis and Treatment

Recent Advances in Electromyography

Electromyography of intrinsic and extrinsic laryngeal muscle activity has been used to investigate peripheral vocal fold paralysis, to diagnose spasmodic dysphonia and to differentiate myopathic from neuropathic disorders. The results have been used to understand the basis of both normal and pathologic speech processes. Bipolar hooked-wire electrodes have been used to investigate laryngeal kinesiology and are increasingly being applied in voice and swallowing investigations. In selected centers, multimodality recordings of simultaneous acoustic, electrophysiologic, aerodynamic and stroboscopic data are being applied to the study of normal and abnormal voicing gestures in individuals with and without dysphonia.

The fabrication and manufacture of implantable devices for pacing the nerves and muscles of the larynx have been accomplished. These devices are transfers of technology already in use in other implantable devices in the body, and they offer new areas for rehabilitation of the paralyzed larynx.

Intraoperative monitoring of laryngeal nerves during thyroid, neck and skull base surgery is being applied to attempt to decrease the risk of injury. Monitoring of the laryngeal and pharyngeal muscles for biofeedback is being done in dysphagia therapy and has important rehabilitation implications for individuals with head injury, neural injury and neuromotor system degeneration associated with the aging process.

Laryngeal and pharyngeal electromyography has had wide clinical application in the diagnosis of and botulism toxin treatment for movement disorders of the larynx and pharynx. For individuals with spasmodic dysphonia, tremor and stuttering, intralaryngeal injection of botulinum type A using electromyography monitoring now offers a new, less invasive treatment.

Chemodenervation with botulism toxin has also been used to treat disorders of the upper esophageal sphincter in selected individuals with dysphagia after stroke and head injury. These ongoing studies offer promise of new treatment for dysphagia.

Acoustic Signal Analysis

The acoustic signal is the most readily available, physical representation of voice and carries all perceptually significant information. Recent developments in technology permit fast and accurate analysis of acoustic signals. Effective acoustic signal analysis continues to be a useful quantitative tool for the evaluation and treatment of voice disorders. Acoustic recording and analysis are now routinely used in voice clinics. New signal processing chips and computer engines now provide clinicians with mainframe computing capabilities, thereby making it easier to quantify the voice. Low-cost digital audio tape technology and digital sound boards enable retrieval of voice samples quickly and accurately for analysis and research.

Imaging

Technologic advances have been achieved in the imaging of the larynx and pharynx. Imaging using real-time magnetic resonance imaging (MRI) has been improved in the last three years. Echo-planar MRI now allows viewing of the laryngeal and pharyngeal structures in the coronal, axial and saggital planes with a sampling time of less than 100 milliseconds. Such applications in the evaluation of pharyngolaryngeal gestures, swallowing dysfunction and voice production problems hold great promise. Ultrasound has been used with increasing success for the evaluation of laryngeal anatomy and function. Scientists have used ultrasound successfully to demonstrate impairment in vocal fold function in the adult and pediatric population.

Imaging of the upper aerodigestive tract is currently most often performed with videofluoroscopic techniques. Combining videofluoroscopic imaging with various physiologic and electrophysiologic measures is now easily performed. These measures include videofluoroscopy and multichannel manometry in the study of swallowing and voice production. Laryngeal electromyography, airflow and videostroboscopy can now be combined with videofluoroscopy. Advances in signal acquisition and computer enhancement will likely reduce radiation dosage. Research should continue in all of these technologies to promote a greater understanding of the complex interactions of the upper aerodigestive tract.

Direct visualization of the laryngopharyngeal region continues to improve with advances in fiber-optic endoscopes and rigid telescopes. The widespread application of this technology has improved patient care and provided the means for direct observation of the larynx and pharynx. Further improvements should be pursued in this technology in the areas of image quality and analysis. Better techniques to quantitate three-dimensional laryngeal images and their changes through the glottal cycle must be developed, and meaningful applications of these images should be used in research and clinical settings.

Visualization of the larynx and its vibratory characteristics using videostroboscopy remains the most valuable tool for the assessment of vocal production and dysfunction. Quantification of the laryngeal image to correlate with other physiologic modalities should remain a high priority.

High-speed photography of the larynx with digital storage has been used to study problems such as voice break, diplophonia and those during voice onset gestures. These findings are being correlated with other physiologic data and hold promise for expanded clinical applications.

Various projects are exploring the use of laser light properties to track mucosal wave characteristics and to estimate absolute laryngeal image size. With lowering costs of computing, digital image analysis of laryngeal motion and vibratory function is now commercially available. The validity of these approaches should be verified. Advances also have been made in the use of radionuclear imaging for evaluating aspiration and swallowing function; such applications hold promise for better evaluation of aspiration and dysphagia.

Dynamic imaging during the formulation and production of language, voice and speech, which is based on increased blood flow during activation of areas of the brain involved in these functions, is under investigation through the use of positron emission tomography (PET). Functional imaging of the brain with MRI techniques also holds promise for such investigations. Differences in flow in certain regions of the two hemispheres of the brain have been identified in the development of sign language, in people who stutter, and following stroke. MRI angiography offers another potential tool for these studies. Fast spin echo MRI techniques have been used to reconstruct the vocal tract to study the effect of alterations in the supraglottic larynx on voice production and swallowing. These methods should be used to study other conditions, and new methods should be developed for imaging of the central nervous system in the study of voice, speech and language.

Improvements in the resolution of static computerized tomography (CT) and MRI have facilitated detection of the presence and extent of congenital and acquired lesions of the larynx, including neoplasms, inflammation and trauma. Two- and three-dimensional imaging have improved modeling for reconstruction of laryngeal trauma and planning of radiotherapy fields. Parameters have been defined for early diagnoses of nonpalpable regional lymph node metastases and correlation with clinical and pathologic findings. The clinical indications for these procedures and the utility of these results require further study.

PET and scintigraphy with radiolabeled monoclonal antibodies specific for tumor-associated antigens have been used to image malignant neoplasms of the upper aerodigestive tract, including the larynx and regional metastases. Improvement is needed in the sensitivity and specificity of these methods, and their potential role in diagnosis, staging and therapy should be determined.

Observations obtained by using a combination of these technologies should be correlated with each other and with measures from nonimaging techniques to develop appropriate models for understanding voice production.

Augmentative and Alternative Voice Sources

Augmentative or alternative communication can replace the speaking mechanism in congenital and acquired disorders of the larynx.

Advances have been made in the development of electronic communication aids, artificial larynges (external, internal and implantable) and in tracheoesophageal shunts (with and without alloplastic voice prostheses). Further study in this area is required. Also needed are efficacy studies to evaluate the relative benefits of these prostheses and to predict which prostheses are appropriate for various populations.

There has been increased recognition of the need for better augmentative communication devices in communicatively disadvantaged populations (low birth weight infants, individuals in the aging population and stroke victims). Advances have been made in augmentative communication devices for the postlaryngectomy population.

One of the major purposes of communication is to express affect or emotion. In the development of augmentative and alternative communication devices and aids, research is needed to develop more normal vocal quality so that the full meaning of vocal communication can be expressed.

There are now augmentative communication systems that have the ability to produce varied voices with multiple pitch ranges. New software has given augmentative communication users the ability to produce speech at a rate similar to that heard in normal conversation; the software incorporates a word prediction program that helps to speed the production of artificial speech. Improvement in the portability of augmentative communication devices provides users with a greater freedom of movement.

There has been increasing interest in forms of augmentative communication for individuals with autism. Further research into the effectiveness and validity of facilitated communication must be undertaken. Studies should be performed to evaluate ways of improving communication in the autistic adult and child.

As the mortality rate in low birth weight infants decreases, the consequences of aggressive intervention becomes apparent. Additional research is needed in ways to improve communication in certain populations, such as low birth weight infants, individuals with tracheostomies and the aged, who are at risk for significant alterations of voice production. Further research is needed to improve the use of augmentative communication in the pediatric population.

Surgical Technology

Recent methodologic developments have given surgeons the potential to alter the structure and improve the function of the larynx reliably. Investigation into the individual controlling variables of voice production has led to a better understanding of disorders of voice production and their treatment.

Phonosurgery enables surgeons to alter the laryngeal framework and its muscular function to improve vocal function. Laryngoplastic phonosurgery is designed to change the laryngeal framework to improve vocal function, and endoscopic phonosurgery of the vocal folds is designed to improve the voice. There have been advances in improving surgical technique in both areas. Research is needed to address the role of these technical advances and the outcome of laryngeal phonosurgery.

Improvement continues to be achieved in the use of laryngotracheal reconstruction, as measured by successful decannulation, to treat congenital and acquired laryngotracheal stenosis. However the effect of laryngotracheal reconstruction on vocal quality deserves further investigation. Research must address uniform methods for reporting voice and speech results in the pediatric population.

Surgical technology continues to advance with the refinement of instruments available for surgery of the vocal fold and the expanded use of lasers for treatment of vocal tract disorders. Newer laser wavelengths and the expanded use of existing lasers have led to improvement of surgical technique and reduction of complications such as scarring and abnormalities of vibratory function. Advances in the anesthetic management of patients have produced a variety of laser-safe endotracheal tubes, as well as improvements in anesthetic techniques that make possible more precise surgical control.

Intraoperative monitoring of the recurrent and superior laryngeal nerves as well as intraoperative monitoring of the voice during phonosurgery have helped to improve surgical outcomes.

There have been new developments in the fabrication of implantable electrode arrays for stimulation of the posterior cricoarytenoid muscle. These new devices offer promise as a tool for adjusting the servomechanism of the larynx. This technology has important potential applications. Implantable devices also are being developed in several major centers for rehabilitation of the paralyzed larynx. These devices with nerve-stimulating cuff electrodes have been implanted with success in animal models, and ongoing study is being carried out with the future goal of implantation in humans.

Aeromechanical and Respiratory Measures

Laryngeal disorders can disrupt the normal pattern of vocal fold valving during speech and affect respiratory patterns and aerodynamic events. For example, vocal nodules, polyps or vocal fold paralysis may change the amplitude and shape of the glottal airflow waveform. These changes in the structure or function of the vocal folds also may change the respiratory and supraglottal aeromechanical activity. Recent studies support consideration of this interaction in the description, diagnosis and treatment of phonatory disorders. To date, few investigators have simultaneously observed speech and abnormal aeromechanical function of the respiratory and laryngeal components. Inverse filtering has made it possible to study the alternating and direct current components of the airflow signal, and this method is being evaluated for its usefulness in differential diagnosis and quantification of the effects of various phonatory treatments.

Behavioral Treatment

The goal of behavioral voice treatment is to maximize vocal effectiveness relative to an existing laryngeal disorder. Behavioral voice treatment may be undertaken (1) as the preferred treatment to resolve a voice disorder when surgery or pharmacotherapy is not indicated, (2) when recommended as the initial treatment in patients in whom medical treatment appears indicated and may obviate the need for surgery or (3) when recommended before and after laryngeal surgery to maximize the postsurgical voice.

Data exist to support the efficacy of techniques of behavioral voice treatment for disorders related to misuse and hyperfunction, medical or physical conditions and psychologic disorders. For example, there are data to support the efficacy of techniques designed to reduce vocal abuse to improve characteristics of the voice and to reduce the recurrence of laryngeal lesions. There are data to support the efficacy of techniques such as musculoskeletal tension reduction to elicit phonation in disorders associated with psychologic stress. Recently, the efficacy of techniques focusing on increased vocal fold adduction and respiratory support has been established in the treatment of the voice disorder accompanying Parkinson's disease. Although data on the efficacy of behavioral treatment have been obtained from group designs, case studies and retrospective analyses, there is still a need for additional comprehensive studies.

Molecular Biology

Recent advances in molecular biology have revolutionized the approach to many diseases and disorders. It is now possible to identify the regulatory factors that contribute to the causation of many diseases at a subcellular level, thereby facilitating precise diagnosis. For example, many steps in the progression of premalignant lesions can now be distinguished. Defects in development can now be studied at a level never before possible. Gene sequences in the Human Genome Project Database facilitate identifying the genetic basis of hereditary disorders. Knowledge of molecular pathology also opens the possibility of completely new approaches to treatment, such as gene therapy or the modulation of cell-surface receptors to alter cell function.

Psychophysical and Perceptual Measures

A great deal of work in the past has attempted to equate descriptive terms, such as "roughness" and "hoarseness," in the perceptual domain with recorded voice signals in the acoustic domain. Such efforts have been disappointing and appear not to have led to a productive endpoint. There are key parameters that must be taken into account in attempting to relate the acoustic voice signal to the listener's voice-quality ratings. For examples, whether a listener is experienced or naive, and the person's internal standards, for what constitute degrees of abnormal voice quality, will vary. In recent years, there has been renewed interest in assessing the reliability and validity of procedures involved in the use of abnormal speech samples and increased attention has been devoted to the use of synthetic speech stimuli. In addition, psychoacoustic experiments have incorporated complex speechlike stimuli in an attempt to simulate the speech signal more closely while maintaining a high level of control of important acoustic stimuli. The role of phonation in speech intelligibility is now being constructed. The importance of laryngeal participation in articulation of the produced sound is now being recognized more and more.

Measurement of Laryngopharyngeal Gestures

Voice quality is controlled by subtle alterations in the setting or resetting of laryngeal and pharyngeal postures, such as laryngeal height, supraglottic constrictions and agonistic or antagonistic interaction of the intrinsic and extrinsic musculature. In recent years, a variety of techniques have been employed to measure these gestures directly or indirectly using electromyography, electroglottography, photoglottography, high-resolution MRI, inverse filtering, stroboscopic imaging, direct fibroscopic imaging and digital storage.

There has been increased understanding of the range of normal laryngopharyngeal activity because of more prevalent and concurrent use of various types of instrumentation, such as videofluoroscopy and pressure-sensing devices. The understanding of the biomechanics of propulsion of the bolus of food during swallowing has been improved. Also, the use of improved imaging procedures has led to a greater understanding of the various forms of upper airway obstruction.

Program Goals

Normal Structure and Function

The program goals for voice and voice disorders are to support research that will lead to the acquisition of new knowledge of a fundamental and applied nature that will enhance understanding of (1) normal vocal and swallowing mechanisms, (2) disordered vocal and swallowing mechanisms, (3) evaluation processes for disordered voice production and swallowing, and (4) prevention, diagnosis and treatment of disorders of voice production and swallowing.

Broad goals include:

- Foster research that examines the structure and the multiple functions of the larynx and upper aerodigestive tract in an integrated manner.
- Encourage the application of molecular biology and research interactions among molecular, cellular and organ systems biology.
- Support acquisition of a database that fosters the evolution of standards for documentation of the vocal function.
- Facilitate training of scientists to study voice, voice disorders, swallowing and swallowing disorders.
- Solicit and support research using diverse subject groups, including children, women and ethnic groups.

Diseases and Disorders of the Larynx and Upper Aerodigestive Tract

- Support epidemiologic studies of the incidence, prevalence and impact of voice and swallowing disorders, as well as the factors that cause or contribute to vocal and swallowing dysfunction.
- Support molecular biologic studies of the genetics and cell biology of laryngeal and vocal tract development, differentiation and disease.
- Foster research that examines the multiple functions and disorders of the larynx and upper aerodigestive tract in an integrated manner.
- Encourage studies of the efficacy of medical and behavioral treatment of voice and swallowing disorders.

Applications of Technology in Prevention, Diagnosis and Treatment

- Encourage studies of the efficacy and relevance of new technologies in the prevention, diagnosis and treatment of voice and swallowing disorders.
- Support studies that foster objective measurement of the physiologic processes of disease.
- Support the development of guidelines for the diagnosis and treatment of voice and swallowing disorders.
- Support multi-institutional studies of the efficacy and cost-effectiveness of diagnostic and treatment procedures for voice and swallowing disorders.

Research Opportunities

Normal Structure and Function

Anatomy, Cellular and Molecular Biology and Genetics

There is a large gap in current understanding of the species-specific neural circuits in the human brain that control voicing. This gap is of concern because it is possible that some human voice disorders involve neural structures that have evolved recently and for which there are no comparative models. Studying these unique human brain structures using postmortem material poses a difficult challenge. An especially difficult aspect of the problem consists of the long neural tracts that connect various parts of the brain. Established techniques that could be used to look at this problem include gross morphology, light, fluorescent and electron microscopy, molecular and cellular biology, neurochemistry and immunocytochemistry. One strategy that could be pursued would be to define the asymmetries in the cortex and subcortical structures related to voicing. In addition, it could be possible to differentiate the central and peripheral structures that subserve respiration, voicing and swallowing.

Research should be encouraged to explore the anatomy of vocal control by using noninvasive imaging in human subjects. Such research could include the use of functional imaging techniques such as PET and functional MRI. Other techniques that image brain function are magnetoencephalography with superconducting magnets and evoked potentials. Finally, studies should be encouraged that map the cerebral cortex by direct electrical stimulation.

Another large gap in current understanding concerns the peripheral nerve supply to the human larynx. There is a lack fundamental knowledge about the motor, sensory and autonomic innervation of the human larynx. For example, in terms of motor innervation, there is evidence that the superior laryngeal nerve may be contributing motor innervation to the laryngeal muscles. In terms of the sensory nerve supply, the larynx receives perhaps the densest sensory innervation of any structure in the body. However, the course of the sensory nerve supply to the different parts of the mucosa, the types of sensory receptors and the distribution of the receptors in the mucosa are unknown. In addition, the distribution of proprioceptive elements within the muscles and joints of the larynx is also unknown. Finally, the distribution of the autonomic innervation to the larynx is poorly understood. For example, the location of the ganglia of the parasympathetic nerve supply has never been identified. Many of these questions can be answered through the use of existing technology.

A major opportunity for research concerns the structure and biomechanics of the laryngeal muscles during voice production, respiration and swallowing. Within the last decade, it has been found that many muscles previously believed to be single muscles are actually composed of subunits called compartments, which are defined by a variety of anatomic criteria. However, the importance of this concept is that anatomic differences between compartments suggests that these compartments perform different functions. This approach has recently been applied to human laryngeal muscles. Different muscle compartments have become specialized in their structure and muscle-fiber composition. These specializations may reflect a functional specialization for phonation, respiration or vocal fold closure. Further work in this area will refine current understanding of how vocal fold vibration is controlled and of the biomechanics of vocal fold articulation.

There have been few studies applying cellular or molecular techniques to the larynx or the central nervous system areas controlling the larynx. Studies should be encouraged into the molecular specializations of laryngeal muscle fibers, nerves and soft tissues. These studies would provide an opportunity to define the distribution of extracellular matrix molecules, growth factors and growth-factor and hormonal receptors. Cell cultures would permit the study of the effects of modulating these components. This research could be done through changes in culture conditions, such as hormone additions and altered matrix components or through insertion of genes into cells that would express growth-factor receptors, etc. Molecular techniques, including in situ hybridization, have great potential for use in refining the functional anatomy of the central nervous system. There is a need for molecular studies to differentiate functional subgroups of the cortex, subcortical nuclei and brain stem. Research opportunities include the following:

- Study the anatomy of vocal control by using noninvasive imaging in human subjects.
- Use molecular and cellular biological, neurochemical and immunocytochemical techniques to study species-specific neural circuits in the human brain that control voicing, including the definition of asymmetries in the cortex and subcortical structures that are related to voice production.
- Use molecular and cellular biology to study peripheral motor, sensory and autonomic innervation of the human larynx.
- Study the structure and biomechanics of the laryngeal muscles with special emphasis on the identification of muscle subunits (compartments).
- Study the molecular specializations of laryngeal muscle fibers, nerves and soft tissues.

Development and Lifespan Alterations

The development of vocalization and swallowing, gender differences in these functions and changes associated with aging are fertile areas of study. Aerodynamic, acoustic, kinematic and electrophysiologic studies are needed to specify age- and gender-related functional differences. Development of control mechanisms for altering pitch, loudness, vocal quality and vocal efficiency are also areas for future research. The understanding of the embryology and cellular physiology of the vocal system, as well as the biochemical role of growth factors and receptors in laryngeal development is still quite limited. The fundamental basis of these functions could be elucidated by the identification and characterization of the genes modifying or dictating the developmental process. Molecular expression studies would be useful in defining critical developmental patterns. Transgenic and gene knockout mice provide a unique experimental approach to the study of gene expression. Further definition of genetic factors involved in both normal and abnormal development are needed because there are more than 100 genetic conditions associated with vocal impairment. Research opportunities include the following:

- Use molecular expression studies to define the role of genetic factors in normal and abnormal laryngeal development better.
- Use aerodynamic, acoustic, kinematic and electrophysiologic techniques to study the normal development of voicing control mechanisms and to specify age- and sex-related differences in vocal function.
- Continue to delineate the effects of hearing impairment and cochlear implantation on vocal control, with special emphasis on identifying critical periods for vocal learning and rehabilitation.
- Conduct epidemiologic studies on the effects of lifestyle (for example, diet, smoking, exercise, alcohol consumption and drug use) and culture on laryngeal function.

Gender, Lifestyle and Cultural Influences

The development of gender differences in this area should receive more specification. Research is needed to understand the role of androgenic hormones and the ways in which their effects can be prevented or ameliorated. Other areas for potential research include (1) factors responsible for the differential susceptibility of women to certain voice disorders; (2) gender differences in gross, microscopic, and molecular structure and biomechanical properties of the vocal tract and (3) hormonal influences affecting changes in vocal production.

Little is known about the effects of lifestyle or cultural influences on the function of the laryngeal, respiratory and upper aerodigestive systems. Further studies of variables such as diet, smoking, drug use, sexual preference, exercise and alcohol consumption would enhance knowledge of fundamental mechanisms, including maladaptive behaviors that contribute to the development of voice disorders. The resulting data also would facilitate the design of prevention programs and early identification of dysfunction. Research opportunities include:

- Study gender differences in the effects of hormones on the larynx.
- Study gender differences in susceptibility to voice disorders.

Role of Auditory Feedback in the Development and Maintenance of Vocal Control

Individuals with congenital and late-onset hearing impairment may have disorders of pitch and loudness control, as well as distinctive abnormalities in voice quality. Research is needed to specify in greater detail the interactions of the subcomponents of the vocal system, in particular respiration and laryngeal function. Only limited attention has been given to the critical periods for the habilitation and rehabilitation of vocal control in these populations. Attention also should be given to the use of biofeedback and motor learning in teaching vocal control to hearing-impaired individuals.

The effect of cochlear implantation on vocal function in prelingually and postlingually deaf individuals also should be studied further. Research opportunities include:

- Analyze critical periods for habilitation and rehabilitation of vocal control in individuals with hearing impairment.
- Study vocal changes in prelingually and postlingually deaf individuals who have had cochlear implants.

Aging

Anatomic changes occur in the voice-producing structures as they develop, mature and age. Preliminary observations indicate that some of the vocal alterations ascribed to aging are reversible. More research is needed to establish the true nature of aging voice and swallowing changes and to develop techniques to forestall or prevent these changes when they interfere with a person's life or livelihood. In addition, irreversible changes should be understood in depth. Study populations should include normal women and men spanning the age range from 20 to 100 years.

Voice quality typically declines with aging in conjunction with alterations in vocal fold structure. There is a need to study the effects of aging on the molecular and cellular biology of the larynx and associated voice-producing structures. Research is required to evaluate gene expression changes, the cellular mechanisms that lead to these changes and the ways in which such changes may contribute to age-related voice changes.

The selective neuronal death in the brain stem as a consequence of aging should be studied. Study of this problem may provide important insights into understanding changes in voice control, respiratory function, reduced airway protection and bolus propulsion in older people. In some neurogenic diseases, selective reduction in motoneuron pools that modulate speech and breathing have recently been found. Research is needed to determine the degree to which selective cell death owing to aging adversely affects voice, swallowing and respiration.

The process of cell death is a naturally occurring phenomenon in developing systems, in particular in the nervous system. Cell death also occurs in mature cells that activate an apoptotic program, possibly in response to physiologic stress. Identification of the signals of cell stress and the initiation and pathway events of the cell death program would make possible a greater understanding of how to control cell death by either blocking it or stimulating it. Several lines of research indicate that alteration of the cytoskeleton and cellular organization are important events in initiation of the cell death program. Research opportunities include the following:

- Attain a better understanding of the process of cell death and the ways in which it influences the vocal and swallowing function with aging.
- Study the effects of selective neuronal death in the brain stem on the control of voice production and swallowing.
- Identify the basic pathogenic mechanisms underlying age-related degenerative processes in the highly specialized muscles of the larynx and upper aerodigestive system.
- Study the cellular biology of cartilage and joint deterioration as it effects voice production and swallowing in aging.

Muscle Atrophy

Since changes resulting from muscle degeneration, motoneuron death, and cell death can differ among types of skeletal muscles, it will be important to determine the basic pathogenic mechanisms underlying age-related degenerative processes in the highly specialized muscles of the larynx and upper aerodigestive system. Since these changes are likely to be reflected in diminished capacities of the upper aerodigestive system for vocalization, swallowing and respiration, the functional consequences of muscle atrophy should be an area of investigation. Subject populations should include women, children, men and diverse ethnic groups. A research opportunity is:

- Study the pathogenic mechanisms of age-related degenerative processes in laryngeal muscles.

Deterioration of Joints, Ligaments, Membranes and Other Tissues of the Laryngeal, Pulmonary and Secretory Systems

The underlying causes of age-related voice changes, although not well understood, are in part attributable to the histologic changes in the tissues associated with voice production. Comparative anatomic studies of the cricoarytenoid joint have been done to determine whether age-related changes in this structure contribute to voice alteration. Progressive ossification of the cricoid and arytenoid cartilages accompanied by periarticular muscular atrophy and fibrosis have been noted in aged tissues. Changes in vocal fold muscle-fiber types and mucosal thickening in conjunction with histologic changes in laryngeal connective tissues also have been identified. These changes act as contributing factors in voice alteration.

To correct vocal deterioration of the joint by means other than surgery, more information is needed on the cellular biology of cartilage and joint deterioration as it affects voice production and swallowing in the aging larynx. This knowledge may lead to medical or exercise therapy to help slow or reverse the process.

The mechanisms involved in increased stiffness and lack of elasticity as they relate to vocal stress need further attention. Additionally, research is needed to determine how to improve the secretory process leading to better rheology and increased laryngeal efficiency.

The anatomy of the aging larynx has been described in human specimens obtained primarily from cadavers. There has been no detailed study of the aging process in which a more uniform genetic and environmentally controlled background is possible. It would be very useful to collect molecular, cellular and anatomic information from aged larynges of a genetically defined species. Information is needed on the localization of extracellular matrix components, growth factors, oncogene expression and growth-factor receptors. This information should be compared with data collected from normal young adult larynges and related to the reduced ability of the larynx and pharynx to recover from injury with aging and the increased susceptibility of the pharynx and larynx to general weakness and dysfunction when an elderly individual becomes debilitated. Research opportunities include:

- Study further the biomechanical properties of laryngeal cartilages, ligaments, muscles and mucosa.
- Study the mechanical characteristics of the laryngeal joints with special emphasis on attaining a better understanding of the ways in which the cricoarytenoid joint functions in vocal fold opening and closing.

Biomechanics of the Larynx and Upper Aerodigestive Tract during Vocalization, Respiration and Swallowing

Biomechanics of the Larynx

The larynx is, in essence, a biologic transducer that converts aerodynamic power into sound energy. Accordingly, the structural components of this transducer and the types of tissues that make up these components should be studied to understand how this conversion is accomplished. The main components of the larynx are nerve, muscles, ligament, cartilage and mucosa. Quantitative information is needed on all these materials to measure their static and dynamic properties. In addition, important information is needed on the aerodynamics of the larynx, the mechanical characteristics of the laryngeal joints, the contribution of mucus to the vibratory behavior of the vocal folds and the special nature of the vocal fold vasculature. An improved understanding of these factors will make possible the development of more realistic computer models of vocal fold vibration and will lead to better restoration of these factors when they are impaired by disease.

An important opportunity in voice science is to define the biomechanics of the vocal fold. The vibration of the vocal fold in the form of a tissue wave is the sound source in the vocal tract. However, the details of how the sound is produced by the vocal fold vibration are still controversial. As a result, the relationship among the molecular, gross, histologic, and visco-elastic structure of the vocal fold and its vibratory behavior also require further examination.

Other factors that may affect vocal fold vibration include the mucosal layer of the vocal fold, the fluid coating on the mucosa, and the vasculature within the vocal fold. The mucosa plays a critical role during vocal fold vibration, and changes in its thickness and consistency are one of the major causes of dysphonia. Major disruptions of this mucosa heal well without a scar, provided that these disruptions do not extend into the underlying conus elasticus. The role of the mucosal fluid layer in normal phonation is poorly understood. However, when this mucus thickens and adheres to the vibrating surface of the vocal fold, it causes severe dysphonia. Alterations in mucus consistency are common causes of dysphonia in the elderly and voice professionals. Finally, the vasculature of the vocal fold also is poorly understood. The supply of blood to muscles generally increases dramatically with exercise; however, in the vocal fold, small changes in mass can have a dramatic effect on vibration. Indeed, the vibratory mass of the vocal folds does not appear to change during prolonged phonation. On the other hand, increased blood supply to the vocal fold mucosa during laryngitis can cause complete aphonia. Therefore, the anatomy and physiology of the vocal fold circulation represent important areas for research.

In addition to phonation, another major area of laryngeal biomechanics is vocal fold articulation. The vocal folds open during inspiration, close forcefully during swallowing, and alternate between open and lightly approximated positions during phonation. Disruptions of vocal fold approximation, such as occurs during vocal fold paralysis, can have devastating consequences: airway obstruction, aspiration during swallowing and dysphonia. Understanding the biomechanics of vocal fold articulation is therefore important with direct clinical relevance. However, even basic concepts of vocal fold articulation are controversial. For example, there is still uncertainty about the capabilities of the cricoarytenoid joint. Some voice scientists believe that the joint is capable of up to three arcs of motion, others claim two, and still others say only one. A similar controversy persists regarding the cricothyroid joint. These controversies make it difficult to interpret how the laryngeal muscles cause the articulation of the vocal folds or deficiencies occur in disease states. Research opportunities include:

- Study the influence of the vascular supply and mucosal fluid layer on vocal fold vibration.
- Determine the essential elements required for vocal fold oscillation, with a goal toward developing a neolarynx from autologous tissues.

Control of Pitch, Loudness and Vocal Quality

Recently, functional models have been used to enhance current knowledge of the dynamic behavior of the vocal folds. Electromyographic studies have increased understanding of the role of the extrinsic and intrinsic laryngeal muscles in the control of pitch. However, the results of these studies have suffered from a lack of functional integration with pulmonary and perilaryngeal structures. Systematic work on the control of pitch, loudness, register and quality should be continued, using both animal and human models.

Concentrated work is needed on the role and interactions of specific muscles and of their aerodynamic effects. These interactions should be related to changes in the glottal configuration, length, shape and forces acting on vibrating structures. Studies should consider laryngeal function and the interaction of the larynx with the dynamics of the entire upper aerodigestive tract and lower respiratory tract. The covariation of intensity and frequency as it relates to subglottal pressure should receive further work. In addition, work in these areas should be extended to encompass subject groups that include women, children and diverse ethnic groups.

Delineation of the acoustic-to-perceptual transform is needed as a basis for better understanding voice-quality disorders. When combined with traditional psychophysical procedures, technologic advances in signal analysis, control and synthesis will be useful in determining those aspects of the voice signal that give rise to the perception of various voice qualities, including disorders. Research opportunities include:

- Continue studying mechanisms of pitch, loudness, quality and register control using both humans and comparative models.
- Delineate the acoustic-to-perceptual transformation with special emphasis on identifying those aspects of the acoustic signal that give rise to the perception of various voice qualities, particularly disordered voice quality.

Vocal Tract Component Interactions

The interactions among phonation, respiration, swallowing and articulation are important. Research should stress the role of the respiratory system as an energy source for the voice. Further study should be given to acoustic and biomechanical interactions, including the effects of vertical movements of the larynx and source-filter effects related to adjustments in the pharynx. Additional demands, such as increased loudness, may bring additional loads to the system. Although such demands have been studied, they must be more clearly defined for different types of vocalization, as in whispering or breathy phonation or as a coping strategy accompanying a disease state. In addition, the role of changes in supraglottic and subglottic acoustic and aerodynamic pressures in vocal function and training could be better understood if the neural sensors that help control the process were more clearly defined.

The dynamic behavior of the larynx and its role as an articulator in speech should receive further attention. Studies focused on the control of timing of laryngeal behavior in coordination with respiratory and articulatory activity may shed considerable light on communication disorders. A research opportunity is:

- Continue to increase research emphasis on the control and timing of laryngeal behavior in coordination with respiratory and articulatory activity.

Swallowing

Basic aspects of swallowing function are beginning to be understood, but additional research is needed to elucidate more fully the swallowing mechanisms. More research is needed on the effects of various bolus types and on using various voluntary controls on systematic changes in laryngeal and pharyngeal function during swallowing. The results of this research will be useful in the evaluation and treatment of individuals with dysphagia.

There is a paucity of information on normal infant swallowing, including details concerning the influence of structural maturation on the swallowing function's transition from infant to adult mechanisms. Such normative information is critical to improving swallowing diagnostic procedures for the infant population.

Efforts to understand the effects of the normal aging process on swallowing should be continued and expanded. This work is particularly critical given the increasing average age of the population and the higher incidence of swallowing difficulties in the elderly.

There should be continued efforts to develop nonradiographic methods for evaluating swallowing function. Such methods would have wide clinical appeal for cases in which repeated evaluations of swallowing are needed to assess treatment-related progress.

Much work remains to be done in determining the details of peripheral and central neural control of swallowing. Studies of peripheral and central mechanisms controlling laryngeal and pharyngeal transitions among respiration, swallowing and phonation are also relevant to the management of dysphagia.

Research is needed to establish a database on the anatomy of human swallowing structures. This database should include information on the exact innervation of each muscle, the internal structure and biomechanics of swallowing structures and the distribution of sensory structures. Research opportunities include:

- Conduct more research on the effects of various bolus types and on using various voluntary controls on systematic changes in laryngeal and pharyngeal function during swallowing.
- Collect more information on normal infant swallowing, including details concerning the influence of structural maturation on the swallowing function's transition from infant to adult mechanisms.
- Continue efforts to develop nonradiographic methods for evaluating swallowing function.
- Determining the details of peripheral and central neural control of swallowing.
- Establish a database on the anatomy of human swallowing structures, including the exact innervation of each muscle, the internal structure and biomechanics of such structures and the distribution of sensory structures.

Comparative and Theoretical Models of Voicing

Comparative Models

Much of the information currently available on the neural control of the larynx has come from comparative studies. The strategies regarding the use of comparative models in research overlap practically all aspects of voice research. Some general themes can be delineated.

Experiments on neural control of voicing should integrate information from structure and function. Research should be encouraged that examines voicing as a complete system from the cellular level to the acoustic output.

Research should be performed that differentiates the structure and function of vocalization, respiration and swallowing. One of the major problems in studying voicing is that the same central and peripheral structures also are responsible for performing two entirely different functions, swallowing and respiration. This fact makes it difficult to design experiments to study any of these functions. Research should be encouraged that defines central or peripheral structures that are purely dedicated to these functions. Experimental strategies might include studying the distribution of sensory receptor types, compartments of laryngeal muscles, functional subnuclei in the nucleus ambiguous and the localization of these functions in cortical and subcortical structures. A research opportunity is:

- Delineate species-specific differences in voice and swallowing structures and functions through the use of comparative studies.

Computational Analysis, Modeling and Speech Synthesis

Additional work is needed to improve the accuracy of laryngeal models. Contemporary models simulate laryngeal biomechanics primarily by using a few elements. It may be necessary to increase the number of elements to simulate laryngeal biomechanics in detail. Eventually, a finite element approach may be necessary to develop a comprehensive, realistic model of the larynx and vocal fold vibration. Modern computers are now powerful enough to achieve highly advanced system simulations. It would be desirable to use fully emerging, computational tools in modeling the larynx. Successful modeling also requires indepth understanding of many delicate, physical properties of the larynx, such as muscular elasticity and surface tension within the larynx.

Voice-quality control continues to be a core area of voice science with multiple areas of application that range from speech development and voice disorders to speech technology. To be able to specify voice characteristics from a functional communication point of view, it is necessary to develop effective descriptive systems for representing the extralinguistic specification of utterances (including emotional elements), as well as linguistic specification that include prosodic information. An appropriate characterization of voice quality and its disorders also would be expected to provide useful information leading to the improvement of a physiology-based model of the larynx.

As a physical phenomenon, vocal fold vibration has received some attention in connection with the concept of physical chaos, a deterministic but apparently random process. This point of view may hold promise for understanding the basic nature of voice production and may provide new insights into the nature of voice-quality differences. A research opportunity is:

- Improve the accuracy of computationally based laryngeal models, perhaps through the use of finite element approaches.

Exceptional Vocal Behavior

Trained vocalists (singers, actors, etc.), particularly those who are considered "gifted" or "exceptional," should be studied because they provide a means of examining the maximum capabilities of human voice production and perception. Information about maximum vocal capabilities may be applied to improving methods of evaluating and treating voice disorders in nonsingers. Areas of particular interest in the study of the trained voice include mechanisms of vocal control and efficiency, predisposing factors for superior vocal performance, vocal endurance and aging effects.

Information about the mechanisms that underlie the superior vocal control and efficiency of trained voices should be potentially useful in helping to clarify voice therapy treatment concepts. For example, attention should be given to determining the extent to which vocal efficiency is dependent on laryngeal factors, vocal tract characteristics and interactions between the laryngeal sound source and vocal tract.

Information concerning the extent to which superior vocal function (performance) is attributable to innate structural factors versus vocal training would be valuable in helping to assess the potential that individuals have for improving voice production. This information not only could be useful for singers but also could be applied in assessing the potential for voice therapy approaches to improve disordered voice production. Also applicable to this general issue would be information concerning the role of genetics in superior vocal function.

The ability of many trained vocalists to perform long and demanding vocal tasks without laryngeal injury is not well understood. A better understanding of the mechanisms that contribute to vocal endurance (and endurance limitations) in trained vocalists could provide important insights into concepts of vocal strain and the roles of voice use and voice abuse in voice disorders. Research opportunities include:

- Continue to study exceptional vocal behavior (for example, in singers), with particular emphasis on mechanisms of vocal control and efficiency, predisposing factors for superior vocal performance, vocal endurance and aging effects.
- Investigate the nature, variability and the effects of overuse on the professional speaking and singing voice.

Diseases and Disorders of the Larynx and Upper Aerodigestive Tract

Population- and Outcome-Based Research

Population-based research is needed to determine the number of persons in the general population who are affected by disorders of the vocal system and the variables that influence the severity and outcome of these disorders. Such studies should include variables related to culture, race, gender and age factors for specific subpopulations. Data on voice usage among different cultures and languages should be explored. Data on prevalence and risk factors may assist in identifying the causes of vocal and swallowing disorders that remain unknown. Multiple research opportunities include the following:

- Promote vocal health awareness in the public.
- Develop data on prevention, diagnosis and therapy of voice disorders. These data are needed on the incidence, prevalence, risk factors and outcome measures of therapy for congenital and acquired voice disorders. These studies should include measures of dysfunction and disease severity and development of a staging system for evaluating common voice disorders.
- Determine the effects of age, gender, race and culture on the incidence, prevalence and outcomes of treatment for diseases and disorders of voice production and swallowing, including cultural differences in diet, health care, behavioral patterns and lifestyle, as well as individual factors.
- Determine the effects of environmental factors on disorders of voice production and swallowing.
- Conduct epidemiologic studies into misuse and abuse disorders, including prevalence, risk factors, environmental effects and efficacy of treatment and management.
- Conduct population-based longitudinal studies. There are only limited data available on the capability of the vocal folds to withstand the demands of daily voice use without injury. The impact of voice loss in certain professions is much greater than others. Preventive maintenance of vocal health in highly vocally demanding professions may be an alternative to the more traditional delivery of health care.
- Efficacy studies should be conducted on the various diagnostic tools available for laryngeal function testing. Currently there are multiple laryngeal function measures that may have diagnostic validity. There is a need for the establishment of commonly agreed upon clinical guidelines for application of these tools in evaluation of affected individuals.

Currently, counseling specific to a given vocal disorder is within the scope of practice of voice clinicians. The challenge of assessing and treating psychogenic voice disorders rests in the interdisciplinary nature of the causes and development of the aberrant voice. Research is needed to permit clinical identification of the psychogenic components in the development and manifestations of a vocal disorder and to determine how psychologic factors influence treatment outcome. Research also is necessary to set standards for counseling skills among voice therapists and to develop guidelines for referrals to professional psychotherapists.

- Investigate the outcome of methods used for prevention, early diagnosis and therapy for specific disorders. There is a need to establish a cost-effective, high-quality approach to treating the various disorders of the vocal system. The costs of the assessment must be balanced by the likelihood of benefits. The establishment of these guidelines may be based on meta analyses or other large multi-institutional collaborative studies.

Congenital and Acquired Structural Lesions

Congenital Abnormalities of the Larynx and Vocal Tract

Considerable research is required as a basis for considering prevention of congenital abnormalities of the larynx and pharynx. Prevention will depend on better understanding of the genetic molecular factors that control the development of the larynx and pharynx. Presently, no animal models exist to aid investigators in the study of these problems. The differentiation of genetic and environmentally induced laryngeal and pharyngeal anomalies is important but poorly understood. There is need for basic studies of the molecular biology of the developing laryngeal and upper respiratory tract structures. Little is known about genetic influences on laryngeal function and dysfunction. Studies in these areas are essential to understand and prevent congenital abnormalities. A research opportunity is:

- Study the genetic and molecular basis for laryngeal and upper aerodigestive tract disorders. These studies should include research on genetic and environmental interactions in congenital abnormalities.

Neoplasms

Patients at high risk for developing head and neck carcinomas include people over the age of 50 with a history of smoking more than 30 packs of cigarettes per year. There is a need for research and outcome studies on smoking cessation. Individuals at high risk may represent a select population for laryngeal cancer screening. Identification of cancers at an earlier clinical stage would greatly increase the cure rate for these tumors. However, a screening process requires careful design so that it has relatively high sensitivity and specificity and moderate cost.

There are many research opportunities in understanding, preventing and treating neoplastic diseases. They include the following:

- Determine the molecular basis for malignancy of the head and neck. Important progress has been made in identifying markers that may reflect key factors in the control of malignant transformation of cells. Extensive studies will be required to define the natural history of malignant cell progression in the vocal tract. Research is needed to define the prognostic value of particular markers before broad screening programs can be considered.
- Investigate chemopreventive agents. Thousands of individuals who are at high risk of developing laryngeal carcinomas are now candidates for chemoprevention protocols following curative therapy for a primary head and neck cancer in an attempt to diminish the likelihood of their

developing a second one. The effects of current and new chemopreventive agents on the larynx are unknown, but the action of such agents is an important area of research.

- Conduct studies that refine and develop the most effective means of treatment of laryngeal and pharyngeal cancers, as well as of other common laryngeal disorders. They should include basic research on the factors that control epithelial cell differentiation and growth, (for example, interaction of retinoids with their receptors) and how these factors are disturbed in carcinogenesis. Studies also are needed to understand and modulate immune functions in this disease. Long-term research should assess recurrence rates, effects of treatment, the effects of cofactors such as smoking and voice abuse and chronic laryngeal irritation.

- Conduct carefully controlled objective analyses of the results of therapeutic options for treatments of carcinoma of the larynx. Approximately 50 to 75 percent of all individuals with head and neck cancer in the United States receive radiation as part of their treatment. Yet there is relatively little information available regarding the effects of irradiation on laryngeal function. However, with the advent of advanced techniques for laryngeal study, measurements of vocal fold vibration and analysis of acoustic parameters, there now exist opportunities for more objective analysis of radiation effects on the larynx.

Viral Infections

Recent research advances have resulted in a better understanding of latent papillomaviruses and Epstein-Barr viruses, including a definition of viral gene expression during latency that may lead to therapy to prevent activation and subsequent disease. Regulation of viral expression during active infection also is at the forefront of current research. A number of factors regulate expression of viral genes that are responsible for the formation of papillomas and carcinomas. Research opportunities include the following:

- Investigate mechanisms whereby intrinsic and extrinsic factors interact with viruses to modify cell growth and differentiation to cause benign and malignant neoplasms.

Inflammatory Disease of the Vocal Tract

Research is needed to improve the understanding of inflammatory diseases of the larynx and upper aerodigestive tract. Pharyngitis and laryngitis affect nearly all Americans at some time and cause hoarseness and dysphagia that range in severity from local irritation to irreversible tissue damage. The results of research on prevention, early detection and intervention should help to limit the effects of these diseases. Endoscopic diagnostic and surgical techniques represent important technical advances, but studies are needed to enhance long-term therapeutic benefits. Research opportunities include the following:

- Study the processes of inflammation and wound repair specific to diseases of the vocal and swallowing systems. This research should include studies of pathophysiology, prevention, detection and intervention.

- Design studies to produce new methods of diagnosis and new treatments for inflammatory diseases of the vocal tract, including infectious and allergic disorders. There is need for research on better diagnosis, assessment and treatment of chronic laryngitis and its relation to gastropharyngeal reflux. Long-term studies of the effects of chronic laryngitis should assess the impact of this disorder.

Trauma, Wound Healing and Treatment of Scarring

Basic information is needed on the pathophysiology, prevention, assessment and treatment of voice problems associated with laryngeal surgery and injury. The study of various strategies used in clinical practice to control or influence wound healing need to be expanded. There is a lack of standardization of specific therapies for particular traumatic defects. Recent advances in medical technology have produced a growing population of children with chronic illness who require prolonged airway management. Long-term tracheostomies have been shown in a canine model to cause disturbance of respiratory reflexes. Further research is needed to investigate voice and laryngeal movement disorders in children and adults with long-term tracheostomies. Research opportunities include the following:

- Develop basic information on the management of trauma and wound healing, including laryngeal surgery and the sequelae of airway maintenance with endotracheal intubation and tracheostomy. These studies should include research on pathophysiology, prevention, assessment and treatment to maximize function.

- Conduct studies of scarring. A serious unsolved problem in the care of individuals with acquired scarring of the larynx after surgery or after trauma is glottic, subglottic and tracheal stenosis. The molecular factors involved in wound healing and scar tissue contracture are not understood. There is a need for research on better methods of airway support and stenting during the healing process. Research is also needed on better means for preventing trauma to the larynx and trachea from endotracheal intubation.

Neural Lesions and Disorders

There is need for research on the factors that influence reinnervation of the laryngeal structures. Although there are now several new techniques available for vocal fold augmentation and for structural modifications of the larynx to improve voice function, there is a lack of adequate knowledge of what surgical procedures should be attempted to ameliorate any given disorder. Better information is needed on the biomechanical effects of specific phonosurgical procedures. This information needs to be integrated with research on the biomechanics of specific laryngeal disorders. Research opportunities include:

- Conduct research into the pathophysiology of neural lesions that result in disorders of voice production and swallowing. This work should include neuropharmacologic and behavioral studies, studies of differential impairment across motor systems, nerve-regeneration studies, identification of markers for early diagnosis and research into dystonias and dyskinesia.

Peripheral Disorders

Peripheral nerve injuries may affect the larynx and upper aerodigestive tract. There is a need for carefully documented studies of the physiology of specific peripheral lesions. One of the most common injuries is to the recurrent laryngeal nerve, which results in vocal fold paralysis. This injury occurs most frequently during operations on the skull base, neck or mediastinum. Tumors, radiation treatment or infections along the path of the vagus nerve also can interrupt laryngeal function, producing alterations of phonation, airway protection and respiration. In bilateral paralysis, the consequences are often devastating. Treatment to date typically causes severe voice deficits but enable the affected individuals to breathe. However, more data are needed to define specific effects of surgical and behavioral treatments for vocal fold paralysis. Research opportunities include the following:

- Carry out additional clinical trials to determine the efficacy of surgical procedures to improve the ability to diagnose and treat these life-threatening conditions. Studies should include the investigation of vocal fold augmentation, thyroplasty, arytenoidectomy, cordotomy, selective reinnervation and electrical pacing.
- Conduct nerve-regeneration studies, needed as a basis for understanding the pathogenesis of peripheral disorders and for developing new forms of treatment. Molecular biologic studies of nerve regeneration are needed for a better understanding of idiopathic neuropathies that involve the larynx.
- Conduct research on laryngeal transplantation. Laryngeal transplantation is being explored in experimental animal studies. Major problems such as the appropriate reinnervation of abductor and adductor muscles have been recently approached. However, immune problems remain to be overcome before laryngeal transplantation can become feasible.
- Conduct research to evaluate the contribution of behavioral treatment to improve the voice source independently or in combination with surgical intervention.

Central Disorders

Control of laryngeal functions for breathing, vocalizing and swallowing may be impaired in neurogenic disorders such as Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, multiple systems disease (Shy-Drager syndrome), Huntington's disease, closed or open head trauma (including traumatic brain injury) and stroke. Studies of neuropharmacological and behavioral management of disorders of laryngeal motor control are needed. In particular, knowledge of differential impairment across motor systems may be useful to understand the pathophysiology of these motor control disorders better. Studies of this nature may lead to more effective management (medical, surgical, behavioral or prosthetic) to support speech, respiration and swallowing. Advancements in measurement techniques, including structural and functional imaging techniques, acoustic mapping and instrumental assessment of movement parameters, should be applied to individuals with neurogenic disorders for more quantifiable information on diagnosis, progression and treatment of the disease. Research opportunities include the following:

- Determine the efficacy of current diagnostic and therapeutic procedures for both peripheral and central disorders that affect voice production and swallowing and develop new approaches to these disorders. This research should include examining the efficacy of voice therapy for neurogenic disorders.
- Continue modification and refinement of the role of voice treatment for Parkinson's disease. Emphasis on the role of phonatory source enhancement and generalization to untreated articulation should be explored. Long-term evaluation of the treatment carryover in relation to disease progression is warranted. Application of this voice treatment to other neural disorders should be addressed.
- Clarify the relationship between neuropathology and laryngeal and pharyngeal disorders. Emphasis should be placed on early diagnostic markers and quantifiable differential aspects of neurogenic disorders and disease progression.
- Evaluate the relationship between limb and laryngeal manifestation of disease and response to neuropharmacologic and neurosurgical treatment. Preliminary data support differential manifestation across these diverse systems. Research should address the relationship between these systems of motor control.
- Conduct studies on dystonias. Focal dystonias of the head and neck cause disruption of speaking and swallowing and impair the quality of life. Advances in understanding dystonias (such as spasmodic dysphonia), derived from brain imaging and autopsy studies suggest that dystonias are attributable to brain lesions or biomechanical changes in the basal ganglia. Epidemiologic and case-control studies are needed to identify possible causative factors leading to the onset of this disorder.
- Continue modification and refinement of the use of botulin toxin injections into laryngeal muscles to reduce abnormal patterns of laryngeal muscle activation. Emphasis on optimal dose and placement of injection (which vary among individuals) will produce better guidelines on standards for treatment. Long-term evaluation of this treatment is needed to determine factors affecting efficacy with repeated injections. The mechanism of diffusion of the toxin in tissue should be better understood.

- Explore alternative methods of treating laryngeal dystonias, such as selective deinnervation of the thyroarytenoid muscles.

- Study respiratory dyskinesia (paradoxical vocal fold motion). This disorder is a problem that has recently been identified as a separate entity sometimes associated with asthma. The dyskinesia may affect vocal fold musculature, or any muscle group in the oropharynx. The mechanism for initiation of dyskinesia and the specific structures involved must be better documented. Characterization of specific parameters such as imaging studies with concurrent data on heart rate and pulmonary function are needed to define the nature of this disorder better. In particular, these disorders associated with asthma may be exercise or environmentally induced. Cross-disciplinary studies of these disorders are essential.

Systemic Disorders Affecting the Larynx and Upper Aerodigestive Tract

Many systemic factors affect the vocal system. They include pharmacologic agents, hormonal fluctuations and imbalances, arthritis and other diseases of the connective tissues, genetic keratin synthesis disorders and disorders of the lower airway. Research opportunities include the following:

- Study the effects of systemic disorders such as connective tissue diseases, abnormalities of keratins and disorders of the lower respiratory tract, that negatively impact voice production and swallowing. Such studies should include basic research in pathophysiology and research on current and new methods of management and treatment.

- Study the effects of drugs on the vocal system and swallowing. There has been little direct research on the effects of drugs on the voice or on the interaction of drugs with other forms of vocal therapy, such as surgery or behavioral management. However, pharmacologic agents can negatively affect the voice and swallowing. For example, some blood pressure medications cause severe coughing. Other agents that increase or decrease secretions of the mucous lining of the larynx and upper respiratory tract can impair both voice production and swallowing. Antidepressants cause dry mouth. Anecdotal evidence implicates anti-inflammatory agents or topical corticosteroid sprays in the pathogenesis of vocal fold polyps. There is increased use of immunosuppressing drugs, some of which cause fluid retention in tissues. The effects of chemoprevention agents on vocal tract function should be studied. Further research also is needed into the impact of these and other agents on the vocal system.

- Conduct research into hormonal effects on the vocal system function. Imbalances of hormones may have a potent impact on the vocal system, particularly for professionals who rely on the quality of their voice. Hormonal imbalances can alter the distribution of electrolytes and water within the extracellular compartments of the vocal folds, causing them to become edematous or swollen and changing the characteristics of their vibrations. These changes occur with hypothyroidism, premenstrual syndrome, androgenic hormone-producing ovarian tumors, pregnancy and puberty in boys. They may follow the administration of birth control pills and postmenopausal hormone therapy in women. Studies are needed to determine the underlying molecular mechanisms of these problems and to clarify the best strategies for evaluating and treating affected individuals.

- Study the effects of specific keratin dysfunctions on voice production and swallowing. Genetic disorders of keratin synthesis or function alter the stability of epithelial cells. Even mild contact with the epithelium can cause blistering. Although generally thought of as skin disorders, the keratin disorders also affect the mucosal epithelium.

- Investigate disorders of connective tissues. These disorders clearly have an impact on vocal fold movement, but their effects on the laryngeal function are not well understood. Research is needed to define mechanisms of abnormal function and the best ways to deal with the problems it causes.

- Study problems of the lower respiratory tract (those airway structures below the vocal folds), that directly affect voice production. Emphysema and other pulmonary problems limit the airflow available for phonation. Evidence suggests that a variety of airborne pollutants may contribute to bronchial and laryngeal spasm and to changes in the mucous lining of the lower respiratory tract. Detailed analyses of mechanisms underlying the effects of diseases and disorders of the lower respiratory tract are needed.

Psychogenic Disorders of the Larynx and Upper Aerodigestive Tract

The challenge of assessing and treating psychogenic voice disorders rests in the interdisciplinary nature of the cause and development of the aberrant voice. Research is needed to permit clinical identification of the psychogenic components in the development and manifestations of a vocal disorder and to determine the ways in which psychologic factors influence treatment outcomes. Research opportunities include the following:

- Conduct research to set standards for counseling skills for voice therapists and develop guidelines for referrals to professional psychotherapists. Future investigative efforts in the area of psychogenic voice disorders should recognize the limited current academic training of speech/voice therapists and scientists in abnormal psychology and the psychotherapeutic process. The understanding and use of subtlety, semantics and interpretation skills, as well as displacement and projection of stress are important elements in successful voice therapy and investigation of the use of psychodynamics in voice therapy. Increased knowledge of these skills would be a helpful precursor to research planning.

Misuse and Abuse Disorders

Individuals who suffer from voice disorders that result from misuse of the vocal mechanism may adopt a less-than-efficient way of vocalizing, which, in turn, may lead to changes in the quality of voice produced in addition to vocal fold damage. The voice may be produced with excessive tension, placing stress on the delicate tissues of the vocal folds and may actually cause edema and subsequent tissue changes. Some of these disorders include vocal nodules, chronic laryngitis, vocal fold hemorrhage, muscle tension dysphonia, polypoid degeneration and vocal fatigue. Any behavior or environmental factor that places strain or irritation on the vocal mechanism may cause these deficits. Risk factors include speaking over noise, inappropriate methods of vocal projection, smoke-filled or dry environment, chronic cough, throat clearing and inappropriate habitual speaking posture. Many forms of vocal abuse are associated with disease processes, as in chronic cough in upper respiratory infection or asthma. Research opportunities include the following:

- Conduct studies to achieve a better understanding of the basic anatomy and physiology of the voice-production mechanism and of alterations that occur during vocal misuse and abuse. These studies should include anatomy and histology in elucidating the mechanisms of injury and healing.

- Investigate the tissue-specific effects of chronic edema on the layered structure of the vocal fold as occurs in polypoid degeneration and chronic laryngitis. With the increase in prevalence of asthma in the general population (although abuse may be incidental or compensatory in these individuals), studies should be undertaken to find ways to determine the contribution of compensatory behaviors and reduce their overlay.

- Develop self-monitoring devices that can prevent vocal injury.

- Investigate the effects of pharmacologic agents on the vocal fold mucosa, as well as the effects of toxic agents both in the workplace and in the general environment.

- Conduct additional studies of epidemiologic factors, including prevalence of these disorders. In addition, there should be continued collection of a qualitative and quantitative database for physiologic variables influencing phonatory patterns.

Influencing Variables

Multicultural

With the increasing diversity of ethnic background, cultures, and languages within the United States population, data on voice and voice disorders in specific cultural and ethnic groups are needed to address fully the health needs of the nation. Studies that address the possible contribution of variables among different ethnic groups, such as differences in anatomy and physiology, language and health behaviors, may provide insight into improved ways of diagnosing, preventing and treating voice disorders. The rise in the incidence and death rates for vocal tract neoplasms in African-American and Hispanic-American populations is of growing concern, and research is needed to determine the basis for this recent change. Research is needed to help distinguish vocal differences and voice disorders owing to cultural diversity in the population. With the diversity of lifestyles in the population, there is a need to identify pertinent lifestyle variables influencing the development of lesions of the vocal tract. Research opportunities include:

- Study of multicultural factors in the etiology, pathogenesis, prevention, diagnosis and therapy of voice disorders.

Gender

Given the known differences in male and female anatomy and physiology, research is needed to define the acoustic and perceptual parameters of the voice and susceptibility to voice disorders caused by gender differences. Research is needed to understand the effect of developmental endocrine differences during life changes that differ by gender. Research also is needed to understand the psychosocial and cultural factors related to gender that influence the seeking and allocation of health care for voice disorders.

Aging

Prevention and treatment of voice and swallowing disorders related to aging should be enhanced by a variety of investigative effort. Research opportunities include the following:

- Collect better data on the prevalence of specific voice disorders and contributing factors associated with aging. Research is needed to understand why, in certain populations, children may be at greater risk for voice disorders such as hoarseness, vocal nodules and papillomatosis. Data are needed on environmental influences, personality characteristics and physical behaviors that contribute to voice disorders in children and senior citizens.
- Identify all age-related voice changes and contributing factors, such as change in respiratory support, diet, nutrition, physical and mental health, vocal hygiene and exercise (for example, singing).
- Evaluate the efficacy of voice treatment in reversing and limiting age-related changes in voice. Such work should evaluate the generalized effects of physical conditioning programs as well as specific treatment directed to laryngeal function for their impact on age-related changes in voice. The mechanisms underlying these changes should be studied.
- Determine the influence of the ingestion of certain medicines frequently prescribed in the later years of life on the vocal abilities of senior citizens.

Environment

Given the evidence suggesting the importance of the influence of environmental factors on the voice, identification of the environmental agents in specific geographic areas and occupations could help to facilitate accurate assessment and therapeutic interventions. Research opportunities include:

- Identify environmental toxins by geographic areas and occupations to improve diagnosis and treatment.

Application of Technology to Prevention, Diagnosis and Treatment

Electromyography

With rapidly decreasing costs of computers and computation, the use of image analysis of fluororadiography and videostroboscopy data may be correlated with electromyographic data. Such multimodality investigations offer the possibility of establishing a critical link among muscle activation, the physiology of phonation and the acoustic end-product. Difficulties exist, however, between the potential of electromyography and its practical realization as a common clinical tool. These issues involve clinical experience and interpretation, standardization of the methods of recording, and technical aspects of electrode placement verification.

Study of the laryngeal muscles, their neural control and their relation to voice output is needed. This requirement will be increasingly important as the population ages.

Magnetic and electrical stimulation of the nerves has clinical and research potential in investigations of voice and swallowing disorders. Such applications are already well established in stroke rehabilitation, and these technologies may be transferrable to the diagnosis and treatment of voice disorders. In individuals with progressive degenerative disorders, tremor or paresis, in which difficulty in voicing or swallowing is the primary symptom, laryngeal and pharyngeal electrodiagnosis may be invaluable to differentiate upper motor neuron from lower motor neuron disease. In individuals with voice loss, neuropathic patterns may be differentiated from myopathic patterns through the use of electrodiagnosis.

The role of the intrinsic muscles of the larynx in voicing and swallowing gestures should be studied. With increased clinical expertise, laryngeal muscle activity and its relation to laryngeal function should be better defined. Multidisciplinary collaboration among those skilled in electromyography and speech science should be established to define the relation between laryngeal activation and voice production.

Sensory innervation of the larynx is important for voicing, swallowing and laryngeal protective reflexes. Aspiration in the elderly and infant apnea continue to be difficult clinical problems. They are related to derangements in the sensory reflex arc of the larynx and upper airway. Evoked sensory potential testing should help to elicit these controlling parameters. Technology transfer from auditory and somatosensory evoked potential research should be applied to the larynx and upper airway. A research opportunity is to:

- Develop better electrodiagnosis of voice and swallowing disorders for monitoring disease status and therapy.

Acoustic Signal Analysis

There continues to be a lack of comprehensive understanding of the physical aspects of human voice signals that define perceived differences in voice quality and its disorders. This lack of understanding hinders the effective application of readily available computing and other technology in voice-related research and clinics. For example, the clinical diagnosis and evaluation of the voice are frequently made based on the analysis of acoustic signals by human ears that tend to be subjective and unreliable. Other available measurement techniques tend to be invasive and expensive. The development of accurate and effective techniques of computerized acoustic signal analysis is expected to reduce significantly the inefficiency and cost of voice care and voice treatment.

Current methods of voice analysis primarily emphasize computation of random variations in the fundamental frequency and amplitude of sustained phonation. It is important to refine and standardize these measurements. It is also important to explore new developments in signal processing, particularly those developments that provide appropriate and detailed characterization of voice signals. For example, the recently developed wavelet transformation process makes possible the multiresolution decomposition of the acoustic signal which may be useful in providing meaningful profiles of voice signals. Comprehensive databases of both normal and disordered voices are needed to facilitate the development of acoustic signal analysis-based technology. Research opportunities include:

- Develop new techniques that provide an accurate and detailed profile of voice signals that are critical to voice quality and its disorders.
- Establish a comprehensive database of both normal and disordered voices to facilitate the development of acoustic signal analysis-based technology.

Imaging

Advances in technology have made possible the use of videostroboscopy, high-speed digital imaging and MRI for evaluation of the vocal tract. Further developments in the technology of MRI scanning are progressing at a rapid pace. This technology offers the promise of noninvasive imaging of the upper aerodigestive tract without radiation exposure. The potential for visualization of the three-dimensional relationship of the vocal tract by imaging is being realized. Faster scanning times and new software developments should lead to the dynamic visualization of swallowing and voicing gestures in normal and diseased states.

Further research into expansion of dynamic MRI should be encouraged for applications to voice and swallowing disorders. The simultaneous acquisition of MRI images and physiologic parameters such as electromyographic and acoustic signals should be used to investigate the normal function and disorders of the vocal tract.

Ultrasound has been found to be a useful noninvasive diagnostic tool for the evaluation of vocal tract disorders in adults and children. Further research should concentrate on improving image quality and assessing the possible applications of ultrasound as a diagnostic tool.

High-speed video imaging of the vocal tract is now possible using miniaturized charge-coupled device cameras and mass digital image storage devices. Though used in industry at this time, this technology should be made available for clinical applications such as the visualization and evaluation of laryngopharyngeal gestures.

Standardization of the techniques of flexible and rigid videoendoscopy and stroboscopy is required. There is a need for normative data, as well as data on abnormalities of the voice, during speech and sustained phonation as viewed by flexible and rigid endoscopes. The standardization of parameters such as voice fundamental frequency, intensity and quality is needed to improve consistency in evaluation and treatment. A research opportunity is:

- Determine the range of normal and abnormal laryngopharyngeal behavior for swallowing in terms of timing and magnitude of structural movements.

Augmentative and Alternative Voice Sources

As medical technology advances, there are many more options for the treatment of previously life-threatening illnesses such as cancer, stroke, heart disease and low birth weight. However, the result of aggressive medical intervention has produced an increased population of individuals with temporary or permanent communication disorders as part of their residual deficit. The need for augmentative or alternative voice sources to assist this population is critical to improved quality of life.

Although a variety of communication devices and aids have been developed, individuals utilizing a voice source are limited in the number of voice substitutes available and the naturalness of the vocal quality. Research is needed to develop and make accessible a less-limited repertoire of voices to allow each individual the choice of an acceptable voice. Synthetic voices that retain the quality of a persons former voice should be built into communication devices of the future. Furthermore, improving the dynamic control of vocal quality, as well as increasing the speed of production of artificial speech, through the use of expert systems will enhance communication functions greatly. Research should be undertaken to develop instruments that will provide a wider array of devices capable of producing voices that are gender, age and culturally specific.

The integration of multimedia systems, including virtual reality, should be undertaken to improve the communication abilities of augmentative communication users.

Implantable devices to improve voice production are now in the experimental stage. Further research should be undertaken. Research opportunities include:

- Develop new technologies, such as surgically implantable devices, to augment communication and swallowing after injury or disease.
- Encourage the use of multimedia technology for the enhancement of augmentative communication.

Surgical Technology

Phonosurgery is a promising new development designed to change the voice by adjustments of the vocal structures. This methodology involves surgical technology that includes new surgical procedures, new surgical tools and developments of new implantable devices that restore or augment function. A variety of new surgical tools, devices and techniques are in development for many previously recalcitrant disorders such as unilateral and bilateral vocal fold paralysis, spasmodic dysphonia, benign mucosal disorders, vascular lesions of the larynx and benign and malignant tumors of the larynx. Innovative implantable devices and surgical procedures also are in the process of being developed for swallow dysfunction. They include the use of endoscopic and open surgery to adjust structures, change muscle tension and make compensatory function more accessible.

Laryngeal framework surgery is being expanded. This surgery goes beyond adjustment of the vocal configuration and tension. Investigations of the effects of laryngeal surgical procedures that change mass, tension and force vectors on the vocal folds are needed. Such investigations should be undertaken in cadavers and in sound-producing animals. These methods should investigate the individual elements of the vocal tract that may be adjusted by phonosurgery, as well as the interactive and interrelational aspects among mass, tension and laryngeal size. Furthermore, research on the effects of adjustments of vocal fold mass, tension and symmetry and their effects on vocal fold vibration and acoustic output is needed to refine the principles of phonosurgery.

New clinical procedures of phonosurgery, such as fat injection, laryngoplasty and nerve reinnervation, should be tested in individual centers and in multicenter trials. The impact of these surgical procedures on quality of life should be determined.

Intraoperative monitoring during endomicrosurgery and laryngeal framework phonosurgery is a promising new area for investigation. The opportunity for auditory and physiologic feedback to the phonosurgeon will help to refine the phonosurgeon's capabilities. Opportunities for intraoperative monitoring include development of new technologies to image vibratory characteristics of the vocal folds during surgery and to measure acoustic and other physiologic parameters such as airflow, and glottal contact and tension. These new technologies should be encouraged.

New surgical implant devices are in development for rehabilitation of vocal fold paralysis and neurogenic disorders that affect voice and swallowing. They include the electronic pacing of paralyzed nerves to the larynx and muscle stimulation using pacing afferent loop transducers that control parameters such as airflow, muscle tension and phrenic nerve activity. These devices offer new hope for avoidance of tracheostomy and for improved voice and swallowing rehabilitation. It is anticipated that new applications of biocompatible implants will be developed for voice and swallowing rehabilitation, and such developments in the animal research model and human clinical applications should be encouraged.

New surgical tools are in development for application in vocal tract disorders. The precise application of laser technology offers surgeons an opportunity to do more precise surgery by limiting the injury to the affected area. New laser wavelengths and new laser devices are being investigated for treatment of laryngeal papillomas and vascular lesions of the larynx. This new laser technology offers opportunities to perform less-invasive surgery avoiding the use of general anesthesia and in some cases to undertake office-based intervention.

The development of technology in molecular biology, biotechnology and genetic engineering will have important implications for the diagnosis and treatment of voice disorders. Specific areas of research that need to be addressed are use of these tools for a better understanding of the molecular and cellular structures of the vocal folds with surgical injury and wound healing. Investigation of the unique molecular and cellular structure of the vocal folds and the impact of surgery and trauma on them should be encouraged. Tools are now being used that offer improvement in intervention and that may modify the wound healing process and reduce scarring. Research training is needed to encourage basic science investigators and clinicians to apply these powerful new tools to voice and swallowing disorders.

Finer surgical tools and better visualization are being developed for surgery of the vocal folds. They include the use of virtual reality imaging devices to locate the lesion using magnifying endoscopes and to diagnose malignancy intraoperatively without surgical biopsy. Such advanced technology can have profound applications in surgical intervention for voice and swallowing disorders and should be encouraged.

Progress continues to be made in laryngotracheal reconstruction for the treatment of congenital and acquired laryngotracheal stenosis. However, the effect of laryngotracheal reconstruction on vocal quality and communication should be investigated further. Research should address uniform methods for reporting voice and speech results in the pediatric population.

Research should continue on prevention of surgical injury to the recurrent and superior laryngeal nerves. Progress has been made on the use of intraoperative monitoring during thyroid, neck, spine and intracranial surgery. Investigations of new surgical techniques and prevention methods should be encouraged. Intubation injury and its anatomic sequelae on the larynx and trachea are well known, but more research is needed to prevent development of such injuries. Voice and swallowing rehabilitation with surgical technology after such injuries should be refined. Prevention of anesthesia complications associated with airway management and endoscopic laser surgery should continue. There is a need for coordinated research with allied fields such as anesthesiology and respiratory therapy to develop safer systems for intraoperative and prolonged ventilatory support. Research opportunities include:

- Develop new surgical technology to improve minimally invasive surgery.
- Develop new technology that improves the intraoperative monitoring and prevention of iatrogenic injuries.

Aeromechanical and Respiratory Measures

There is a need for additional information regarding the respiratory and laryngeal interaction and the usefulness of airflow and pressure signals in diagnosis and treatment. Studies should be conducted of the role of subglottal air pressure and its interaction with the activity of the laryngeal muscles in control of pitch and loudness in voice disorders. The relationships among glottal incompetence, aspiration and pulmonary disease should be studied. Multidimensional studies that integrate imaging and aerodynamic measures would offer important information. Standardization of aeromechanical and respiratory measures is needed. It would be helpful to undertake more diverse studies to address aeromechanical and respiratory measures in disordered speakers across age, gender and culture to establish their contribution to diagnosis and treatment. Research opportunities include:

- Obtain more information on the interactions among supralaryngeal, laryngeal, and respiratory structures in acute and chronic effects related to aspiration.
- Develop standardization of recording technology for acoustic, physiologic and imaging information.
- Improve and standardize techniques for measuring vocal disturbances and further investigate the origin and perceptual impact of these measurable vocal disturbances.

Behavioral and Medical Treatment

Enhancing vocal function is critical to improving quality of life. Studies of the efficacy of treatment for voice disorders are essential. The roles of medical and behavioral intervention should be studied independently and in combination. Treatment efficacy should be defined in relation to impact on perceptual characteristics of voice and speech as well as in relation to measures of the underlying physiologic bases. Techniques that enhance treatment efficiency and effectiveness should be identified. To maximize generalizability of findings, future research should include more large-group studies, as well as case study designs. Research opportunities include the following:

- Conduct multi-institutional, randomized clinical trials to determine the efficacy of behavioral and medical therapy for voice and swallowing disorders.
- Evaluate the impact of voice treatment on speech intelligibility in disorders of voice and speech production.

Biotechnology

Recent advances in biotechnology open promising new windows of research. Such tools now can be applied to the diagnosis and treatment of many of the diseases and disorders of the vocal system. Monoclonal antibodies are available to recognize many disease-associated proteins and inappropriate expression of normal proteins. Many more are needed. Genetic engineering can potentially provide reagents for new treatments targeted more specifically to the molecular basis of the disease. There is a need for greater awareness of and the ability to use these new approaches. Research is needed to develop the tools and then apply them to diagnosis, treatment and prevention. Research opportunities include:

- Provide information to clinicians and scientists for application of biotechnology to voice and swallowing.
- Improve technology transfer turnover; encourage and develop new application of technology useful for diagnosis and treatment.

Psychophysical and Perceptual Measures

There are a number of artificial intelligence techniques, such as use of expert systems and neuro-networks, that can be useful for integrating human evaluations with computerized formal algorithmic procedures. In a sense, this is a new research methodology that can supplement or, in some cases, replace straightforward statistical inference in data analysis. This methodology can be particularly effective for quantitatively describing and characterizing complex phenomena such as vocal quality in conversational speech. Although statistical data reduction should be encouraged for quantifying research findings, innovative quantitative methods of data interpretation also should be studied.

Just noticeable differences (JND) should be obtained for small physiologic changes in relation to the ensuing aerodynamic, acoustic, and perceptual chain of events for a better understanding of linkages among these domains. For example, if the glottis is abducted in small increments, what effect does this action have on the volume velocity of air flowing through the glottis, the quality of the changes in the acoustic signal and the quality of the resulting percept? This approach is physiologically driven, rather than perceptually driven, and may lead to natural categories that are more physically determined and less subjectively determined.

Greater use of computerized analysis-by-synthesis procedures should be used. In this fashion, a listener matches the quality of a naturally produced, deviant voice by altering acoustic voice parameters in a speech synthesis program. The resulting acoustic values quantify the listener's auditory impression of the deviant vocal quality. This approach explicitly links acoustic representations to perceived qualities, simultaneously improving the validity of both the perceptual labels of voice quality and the utility of acoustic measures of voice.

There is also a need for better computerized synthesis of pathologic voice qualities. The availability of a database consisting of samples of deviant voice qualities might facilitate the adoption of standardized samples that could be shared in a widespread fashion among scientists and clinicians.

An alternative method of characterizing voice signals as different from normal that appears to show some promise is to use a nonlinear dynamics (chaos theory) approach. Although this approach is being used to investigate the acoustic signal, it might be possible to equate discontinuities in the acoustic signal with categorical differences in the perceptual domain. Research opportunities include:

- Obtain JND data linking physiologic, acoustic and perceptual changes.
- Improve computer-synthesized productions of abnormal voice quality.
- Develop a database consisting of different types and severities of abnormal voice qualities that could serve as a standard for comparison across clinical and laboratory settings.
- Explore greater usage of computerized analysis-by-synthesis technology in linking abnormal voice qualities to perceptual ratings.

Measurement of Laryngopharyngeal Activity

The regulation of contact and fluid pressures in the upper aerodigestive tract is critical in the passage of the bolus to the esophagus. Valving of the tongue against the palate, the soft palate against the pharyngeal walls and other valving maneuvers are all important, but the magnitude and timing of

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these contact pressures are not well understood. Moreover, the balance of fluid pressures between the esophageal seal and glottal seal is important but, again, not well understood. For example, it is not known what minimal pressures are needed to force the bolus through the esophageal entrance while at the same time maintaining glottal closure. Such studies are needed to understand the disorders of swallowing and aspiration in the elderly better.

More information is needed on the range of both normal and abnormal laryngopharyngeal behavior using concurrent instrumentation. Better methods are needed to separate abnormal from normal behavior using available and new clinical instruments. More information is needed on the activity of individual muscles during swallowing and on what actually triggers the swallowing reflex, such as thermal versus mechanical stimulation and the critical sites of such stimulation. Developmental aspects of swallowing need to be investigated. Few biomechanical studies of swallowing activity have been conducted in adults, and even fewer have been conducted in children.

Upward and forward movement of the hyothyroid complex appears to be important in normal swallowing maneuvers. However, it is not well known what compensations occur, if any, when the anatomy and physiology of the mechanism are compromised by the surgical removal of portions of the mechanism such as the hyoid bone or musculature of the floor of the mouth.

More information is needed on the possible interaction between swallowing disorders and speech disorders, especially in individuals with neurogenic impairments. For example, there may be some generalization of treatment effects for people with dysarthria in reducing swallowing problems and vice versa. Also, specific speech disorders, such as excessive breathiness, might be predictive of swallowing complications, such as an inability to close the laryngeal airway thus resulting in aspiration. As another example, weak tongue activity for speech might be predictive of an inability to generate sufficient intraoral pressure during swallowing. Perhaps individuals with a spasmodic type of dysarthria might be better able to generate the increased intraoral pressures needed for swallowing than individuals with a flaccid type of dysarthria. Also, more information is needed on central nervous system control of swallowing and vocalization.

Normal individuals may aspirate to some degree, but little is known about the degree to which aspiration can occur within safe limits; that is, the functional tolerance for aspiration is not well defined. Better coordination is needed between the respiratory therapist and the swallowing therapist regarding such aspects as clearing the lungs and possibly increasing tolerance for low-level aspiration. More information is needed on the chronic effects of aspiration on respiration.

Cervical auscultation is becoming more common as a diagnostic procedure for evaluating swallowing disorders. The reliability and validity of such procedures, as well as other noninvasive techniques, need to be determined. The sites and significance of specific sounds during swallowing should be investigated. Also, different auscultation aids, such as stethoscopes, contact microphones and accelerometers, should be compared.

New imaging methods, such as dynamic MRI, should be used in conjunction with other established methods such as endoscopy and videofluoroscopy to investigate the movement and positioning of the laryngopharyngeal structures during speech and swallowing among individuals with and without abnormalities. Multidimensional simultaneous approaches are advantageous in that the deficiencies of a particular measure may be counterbalanced by the advantages of other techniques. Research opportunities include the following:

- Investigate the magnitudes and timing of contact and fluid pressures occurring in the upper aerodigestive tract during normal and abnormal swallowing maneuvers.
- Obtain more information on peripheral and central nervous system control of swallowing behavior.
- Obtain additional information on the reliability and validity of noninvasive clinical procedures, such as cervical auscultation, in assessing swallowing disorders.

APPENDIX A

Public Law 100-553

APPENDIX A

Public Law 100-553
100th Congress

An Act

To amend the Public Health Service Act to establish within the National Institutes of Health a National Institute on Deafness and Other Communication Disorders.

Oct. 28, 1988
[S. 1727]

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

National Deafness and Other Communication Disorders Act of 1988.
42 USC 201 note.

SECTION 1. SHORT TITLE.

This Act shall be cited as the "National Deafness and Other Communication Disorders Act of 1988".

SEC. 2. ESTABLISHMENT AND TRANSFER OF FUNCTIONS.

Title IV of the Public Health Service Act (42 U.S.C. 281 et seq.) is amended—

(1) in section 401(b)(1)—

(A) by striking "and Communicative" in subparagraph (J); and

(B) by adding at the end the following new subparagraph:

"(M) The National Institute on Deafness and Other Communication Disorders.";

(2) in the heading for subpart 10 of part C, by striking "and Communicative";

(3) in section 457—

(A) by striking "and Communicative"; and

(B) by striking "disorder, stroke," and all that follows and inserting "and disorder and stroke."; and

(4) in Part C, by adding at the end the following new subpart:

Education.
Research and development.
Public information.

"Subpart 13—National Institute on Deafness and Other Communication Disorders

"PURPOSE OF THE INSTITUTE

42 USC 285m.

"SEC. 464. The general purpose of the National Institute on Deafness and Other Communication Disorders (hereafter referred to in this subpart as the 'Institute') is the conduct and support of research and training, the dissemination of health information, and other programs with respect to disorders of hearing and other communication processes, including diseases affecting hearing, balance, voice, speech, language, taste, and smell.

"NATIONAL DEAFNESS AND OTHER COMMUNICATION DISORDERS PROGRAM

42 USC 285m-1.

"SEC. 464A. (a) The Director of the Institute, with the advice of the Institute's advisory council, shall establish a National Deafness and Other Communication Disorders Program (hereafter in this section referred to as the 'Program'). The Director or the Institute shall, with respect to the Program, prepare and transmit to the Director of NIH a plan to initiate, expand, intensify and coordinate activities of the Institute respecting disorders of hearing (including tinnitus) and other communication processes, including diseases affecting hearing, balance, voice, speech, language, taste, and smell. The plan shall include such comments and recommendations as the Director of the Institute determines appropriate. The Director of the Institute shall periodically review and revise the plan and shall transmit any revisions of the plan to the Director of NIH.

"(b) Activities under the Program shall include—

"(1) investigation into the etiology, pathology, detection, treatment, and prevention of all forms of disorders of hearing and other communication processes, primarily through the support of basic research in such areas as anatomy, audiology, biochemistry, bioengineering, epidemiology, genetics, immunology, microbiology, molecular biology, the neurosciences, otolaryngology, psychology, pharmacology, physiology, speech and language pathology, and any other scientific disciplines that can contribute important knowledge to the understanding and elimination of disorders of hearing and other communication processes;

"(2) research into the evaluation of techniques (including surgical, medical, and behavioral approaches) and devices (including hearing aids, implanted auditory and nonauditory prosthetic devices and other communication aids) used in diagnosis, treatment, rehabilitation, and prevention of disorders of hearing and other communication processes;

"(3) research into prevention, and early detection and diagnosis, of hearing loss and speech and language disturbances (including stuttering) and research into preventing the effects of such disorders on learning and learning disabilities with extension of programs for appropriate referral and rehabilitation;

"(4) research into the detection, treatment, and prevention of disorders of hearing and other communication processes in the growing elderly population with extension of rehabilitative programs to ensure continued effective communication skills in such population;

"(5) research to expand knowledge of the effects of environmental agents that influence hearing or other communication processes; and

"(6) developing and facilitating intramural programs on clinical and fundamental aspects of disorders of hearing and all other communication processes.

"DATA SYSTEM AND INFORMATION CLEARINGHOUSE

42 USC 285m-2. "SEC. 464B. (a) The Director of the Institute shall establish a National Deafness and Other Communication Disorders Data System for the collection, storage, analysis, retrieval, and dissemination of data derived from patient populations with disorders of hearing or other communication processes, including where possible, data involving general populations for the purpose of identifying individuals at risk of developing such disorders.

"(b) The Director of the Institute shall establish a National Deafness and Other Communication Disorders Information Clearinghouse to facilitate and enhance, through the effective dissemination of information, knowledge and understanding of disorders of hearing and other communication processes by health professionals, patients, industry, and the public.

"MULTIPURPOSE DEAFNESS AND OTHER COMMUNICATION DISORDERS CENTER

"SEC. 464C. (a) The Director of the Institute shall, after consultation with the advisory council for the Institute, provide for the development, modernization, and operation (including care required for research) of new and existing centers for studies of disorders of hearing and other communication processes. For purposes of this section, the term 'modernization' means the alteration, remodeling, improvement, expansion, and repair of existing buildings and the provision of equipment for such buildings to the extent necessary to make them suitable for use as centers described in the preceding sentence. 42 USC 285m-3.

"(b) Each center assisted under this section shall—

"(1) use the facilities of a single institution or a consortium of cooperating institutions; and

"(2) meet such qualifications as may be prescribed by the Secretary.

"(c) Each center assisted under this section shall, at least, conduct—

"(1) basic and clinical research into the cause diagnosis, early detection, prevention, control and treatment of disorders of hearing and other communication processes and complications resulting from such disorders, including research into rehabilitative aids, implantable biomaterials, auditory speech processors, speech production devices, and other otolaryngologic procedures;

"(2) training programs for physicians, scientists, and other health and allied health professionals; Health care professionals.

"(3) information and continuing education programs for physicians and other health and allied health professionals who will provide care for patients with disorders of hearing or other communication processes; and

"(4) programs for the dissemination to the general public of information—

"(A) on the importance of early detection of disorders of hearing and other communication processes, of seeking prompt treatment, rehabilitation, and of following an appropriate regimen; and

"(B) on the importance of avoiding exposure to noise and other environmental toxic agents that may affect disorders of hearing or other communication processes.

"(d) A center may use funds provided under subsection (a) to provide stipends for health professionals enrolled in training programs described in subsection (c)(2).

"(e) Each center assisted under this section may conduct programs—

"(1) to establish the effectiveness of new and improved methods of detection, referral, and diagnosis of individuals at risk of developing disorders of hearing or other communication processes; and

"(2) to disseminate the results of research, screening, and other activities, and develop means of standardizing patient data and recordkeeping.

"(f) The Director of the Institute shall, to the extent practicable, provide for an equitable geographical distribution of centers assisted under this section. The Director shall give appropriate consideration Aged persons. Children and youth.

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to the need for centers especially suited to meeting the needs of the elderly, and of children (particularly with respect to their education and training), affected by disorders of hearing or other communication processes.

"(g) Support of a center under this section may be for a period not to exceed seven years. Such period may be extended by the Director of the Institute for one or more additional periods of not more than five years if the operations of such center have been reviewed by an appropriate technical and scientific peer review group established by the Director, with the advice of the Institute's advisory council, if such group has recommended to the Director that such period should be extended.

"NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS ADVISORY BOARD

42 USC 285m-4. "SEC. 464D. (a) The Secretary shall establish in the Institute the National Deafness and Other Communication Disorders Advisory Board (hereafter in this section referred to as the 'Advisory Board').

"(b) The Advisory Board shall be composed of eighteen appointed members and nonvoting ex officio members as follows:

"(1) The Secretary shall appoint—

"(A) twelve members from individuals who are scientists, physicians, and other health and rehabilitation professionals, who are not officers or employees of the United States, and who represent the specialties and disciplines relevant to deafness and other communication disorders, including not less than two persons with a communication disorder; and

"(B) six members from the general public who are knowledgeable with respect to such disorders, including not less than one person with a communication disorder and not less than one person who is a parent of an individual with such a disorder.

Of the appointed members, not less than five shall by virtue of training or experience be knowledgeable in diagnoses and rehabilitation of communication disorders, education of the hearing, speech, or language impaired, public health, public information, community program development, occupational hazards to communications senses, or the aging process.

"(2) The following shall be ex officio members of each Advisory Board:

"(A) The Assistant Secretary for Health, the Director of NIH, the Director of the National Institute on Deafness and Other Communication Disorders, the Director of the Centers for Disease Control, the Chief Medical Director of the Veterans' Administration, and the Assistant Secretary of Defense for Health Affairs (or the designees of such officers).

"(B) Such other officers and employees of the United States as the Secretary determines necessary for the Advisory Board to carry out its functions.

"(c) Members of an Advisory Board who are officers or employees of the Federal Government shall serve as members of the Advisory Board without compensation in addition to that received in their regular public employment. Other members of the Board shall receive compensation at rates not to exceed the daily equivalent of the annual rate in effect for grade GS-18 of the General Schedule for each day (including traveltime) they are engaged in the performance of their duties as members of the Board.

"(d) The term of office of an appointed member of the Advisory Board is four years, except that no term of office may extend beyond the expiration of the Advisory Board. Any member appointed to fill a vacancy for an unexpired term shall be appointed for the remainder of such term. A member may serve after the expiration of the member's term until a successor has taken office. If a vacancy occurs in the Advisory Board, the Secretary shall make an appointment to fill the vacancy not later than 90 days from the date the vacancy occurred.

"(e) The members of the Advisory Board shall select a chairman from among the appointed members.

"(f) The Secretary shall, after consultation with and consideration of the recommendations of the Advisory Board, provide the Advisory Board with an executive director and one other professional staff member. In addition, the Secretary shall, after consultation with and consideration of the recommendations of the Advisory Board, provide the Advisory Board with such additional professional staff members, such clerical staff members, such services of consultants, such information, and (through contracts or other arrangements) such administrative support services and facilities, as the Secretary determines are necessary for the Advisory Board to carry out its functions.

"(g) The Advisory Board shall meet at the call of the chairman or upon request of the Director of the Institute, but not less often than four times a year.

"(h) The Advisory Board shall—

"(1) review and evaluate the implementation of the plan prepared under section 464A(a) and periodically update the plan to ensure its continuing relevance;

"(2) for the purpose of assuring the most effective use and organization of resources respecting deafness and other communication disorders, advise and make recommendations to the Congress, the Secretary, the Director of NIH, the Director of the Institute, and the heads of other appropriate Federal agencies for the implementation and revision of such plan; and

"(3) maintain liaison with other advisory bodies related to Federal agencies involved in the implementation of such plan and with key non-Federal entities involved in activities affecting the control of such disorders.

"(i) In carrying out its functions, the Advisory Board may establish subcommittees, convene workshops and conferences, and collect data. Such subcommittees may be composed of Advisory Board members and nonmember consultants with expertise in the particular area addressed by such subcommittees. The subcommittees may hold such meetings as are necessary to enable them to carry out their activities.

Reports.

"(j) The Advisory Board shall prepare an annual report for the Secretary which—

"(1) describes the Advisory Board's activities in the fiscal year for which the report is made;

"(2) describes and evaluates the progress made in such fiscal year in research, treatment, education, and training with respect to the deafness and other communication disorders;

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"(3) summarizes and analyzes expenditures made by the Federal Government for activities respecting such disorders in such fiscal year; and

"(4) contains the Advisory Board's recommendations (if any) for changes in the plan prepared under section 464A(a).

"(k) The National Deafness and Other Communication Disorders Advisory Board shall be established not later than 90 days after the date of the enactment of the National Institute on Deafness and Other Communication Disorders Act.

"INTERAGENCY COORDINATING COMMITTEE

42 USC 285m-5. "SEC. 464E. (a) The Secretary may establish a committee to be known as the Deafness and Other Communication Disorders Interagency Coordinating Committee (hereafter in this section referred to as the 'Coordinating Committee').

"(b) The Coordinating Committee shall, with respect to deafness and other communication disorders—

"(1) provide for the coordination of the activities of the national research institutes; and

"(2) coordinate the aspects of all Federal health programs and activities relating to deafness and other communication disorders in order to assure the adequacy and technical soundness of such programs and activities and in order to provide for the full communication and exchange of information necessary to maintain adequate coordination of such programs and activities.

"(c) The Coordinating Committee shall be composed of the directors of each of the national research institutes and divisions involved in research with respect to deafness and other communication disorders and representatives of all other Federal departments and agencies whose programs involve health functions or responsibilities relevant to deafness and other communication disorders.

"(d) The Committee shall be chaired by the Director of NIH (or the designee of the Director). The Committee shall meet at the call of the chair, but not less often than four times a year.

Reports. "(e) Not later than 120 days after the end of each fiscal year, the Committee shall prepare and transmit to the Secretary, the Director of NIH, the Director of the Institute, and the advisory council for the Institute a report detailing the activities of the Committee in such fiscal year in carrying out subsection (b).

"LIMITATION ON ADMINISTRATIVE EXPENSES

42 USC 285m-6. "SEC. 464F. With respect to amounts appropriated for a fiscal year for the National Institutes of Health, the limitation established in section 408(b)(1) on the expenditure of such amounts for administrative expenses shall apply to administrative expenses of the National Institute on Deafness and Other Communication Disorders.".

SEC. 3. TRANSITIONAL AND SAVINGS PROVISIONS.

42 USC 285m note. Gifts and property. Contracts. Records. (a) TRANSFER OF PERSONNEL, ASSETS, AND LIABILITIES.—Personnel employed by the National Institutes of Health in connection with the functions vested under section 2 in the Director of the National Institute on Deafness and Other Communication Disorders, and assets, property, contracts, liabilities, records, unexpended balances of appropriations, authorizations, allocations, and other funds of the National Institutes of Health, arising from or employed, held, used,

available to, or to be made available, in connection with such functions shall be transferred to the Director for appropriate allocation. Unexpended funds transferred under this subsection shall be used only for the purposes for which the funds were originally authorized and appropriated.

Grants.
Contracts.

(b) Savings Provisions.—With respect to functions vested under section 1 in the Director of the National Institute on Deafness and Other Communication Disorders, all orders, rules, regulations, grants, contracts, certificates, licenses, privileges, and other determinations, actions, or official documents, that have been issued, made, granted, or allowed to become effective, and that are effective on the date of the enactment of this Act, shall continue in effect according to their terms unless changed pursuant to law.

Approved October 28, 1988.

LEGISLATIVE HISTORY—S. 1727 (H.R. 3361):

HOUSE REPORTS: No. 100-761 accompanying H.R. 3361 (Comm. on Energy and Commerce).

CONGRESSIONAL RECORD, Vol. 134 (1988):
Oct. 7, considered and passed Senate.
Oct. 13, considered and passed House.

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APPENDIX B

National Strategic Research Plan Expert Panel Members

PANEL ON LANGUAGE AND LANGUAGE IMPAIRMENTS

Cochairpersons

Dorothy M. Aram, Ph.D.
Professor of Speech Pathology
Division of Communication Disorders
Emerson College
Boston, MA 02116-1596

Eleanor M. Saffran, Ph.D.
Professor
Department of Neurology
Temple University School of Medicine
Philadelphia, PA 19140

Members

Elizabeth Bates, Ph.D.
Professor
Center for Research in Language
University of California - San Diego
La Jolla, CA 92093-0526

David Caplan, M.D., Ph.D.
Associate Neurologist
Neurology Service
Massachusetts General Hospital
Boston, MA 02114

Phil J. Connell, Ph.D.
Chairman
Department of Speech and Hearing Sciences
Indiana University
Bloomington, IN 47404

Dean C. Garstecki, Ph.D.
Head
Audiology and Hearing Impairment Program
Department of Audiology
Northwestern University
Evanston, IL 60208

Aquiles Iglesias, Ph.D.
Professor and Chairman
Department of Speech, Language and Hearing
Temple University
Philadelphia, PA 19122

Richard R. Kretchmer, Ed.D.
Professor
Department of Early Childhood and Special Education
University of Cincinnati
Cincinnati, OH 45221

Diane Lillo-Martin, Ph.D.
Department of Linguistics
University of Connecticut
Storrs, CT 06269-1145

Jon F. Miller, Ph.D.
Professor
Waisman Center
University of Wisconsin - Madison
Madison, WI 53705

Helen J. Neville, Ph.D.
Director
Neuropsychology Lab
Salk Institute
La Jolla, CA 92037

Elissa L. Newport, Ph.D.
Professor
Department of Psychology
University of Rochester
Rochester, NY 14627

Paula Tallal, Ph.D.
Professor and Co-Director
Center for Molecular and
Behavioral Neuroscience
Rutgers University
Newark, NJ 07102

Orlando L. Taylor, Ph.D.
Interim Dean
Graduate School of Arts and Sciences
Howard University
Washington, D.C. 20059

Bruce Tomblin, Ph.D.
Professor
Department of Speech Pathology
and Audiology
Wendell Johnson Speech
and Hearing Center
University of Iowa
Iowa City, IA 52242-1012

Liaison to the National Deafness and Other Communication Disorders Advisory Board

Paula Menyuk, D.Ed.
Professor
Developmental Studies
School of Education
Boston University
Boston, MA 02215

Resource Persons

Allen E. Boysen, Ph.D.
Director
Audiology and Speech
Pathology Service
Department of Veterans Affairs
Washington, D.C. 20422

William E. Castle, Ph.D.
Vice President, Government Relations
Director
Rochester Institute of Technology
National Technical Institute for
the Deaf
Rochester, NY 14623-0887

G. Reid Lyon, Ph.D.
Psychologist
Human Learning and Behavior Branch
National Institute of Child Health
and Human Development
National Institutes of Health
Bethesda, MD 20892

Donald S. Moores, Ph.D.
Director
Center for Studies on Education &
Human Development
Kendall School
Gallaudet University
Washington, D.C. 20002

NIDCD Staff Liaison

Judith A. Cooper, Ph.D.
Deputy Director
Division of Communication Sciences
and Disorders
National Institute on Deafness and
Other Communication Disorders
National Institutes of Health
Bethesda, MD 20892-7180

Mr. Howard J. Hoffman
Chief
Epidemiology, Statistics
and Data System Branch
National Institute on Deafness and
Other Communication Disorders
National Institutes of Health
Bethesda, MD 20892-7180

PANEL ON BALANCE AND BALANCE DISORDERS

Cochairpersons

Fay B. Horak, Ph.D.
Senior Scientist
R.S. Dow Neurological Sciences Inst.
of Good Samaritan Hospital
and Medical Center
Portland, OR 97210

Joseph B. Nadol, Jr., M.D.
Professor and Chairman
Department of Otolaryngology
Massachusetts Eye & Ear Infirmary
Boston, MA 02114

Members

Alvin J. Beitz, Ph.D.
Professor
Department of Veterinary
Pathobiology
University of Minnesota
St. Paul, MN 55108

David P. Corey, Ph.D.
Associate Professor
Department of Neurology
Massachusetts General Hospital
Boston, MA 02114

Manning J. Correia, Ph.D.
Professor
Departments of Otolaryngology
and Physiology and Biophysics
University of Texas Medical Branch
Galveston, TX 77555

Jay M. Goldberg, Ph.D.
Professor
Department of Pharmacological and
Physiological Sciences
University of Chicago
Chicago, IL 60637

Gay R. Holstein, Ph.D.
Assistant Professor
Department of Neurology
Mount Sinai School of Medicine
New York, NY 10029

Steven F. Myers, Ph.D.
Assistant Professor
Department of Biology
University of Michigan - Flint
Flint, MI 48502-2186

Gary D. Paige, M.D., Ph.D.
Unit Chief
Department of Ophthalmology
and Neurotology
University of Rochester
Medical Center
Rochester, NY 14642

Ellengene H. Peterson, Ph.D.
Associate Professor
Department of Biological Sciences
Ohio University
Athens, OH 45701-2979

Phillip A. Wackym, M.D.
Assistant Professor
Goodhill Ear Center
Division of Head and Neck Surgery
UCLA School of Medicine
Los Angeles, CA 90024-1794

Victor J. Wilson, Ph.D.
Professor
Department of Neurophysiology
Rockefeller University
New York, NY 10021

Billy J. Yates, Ph.D.
Assistant Professor
Neurophysiology Laboratory
Rockefeller University
New York, NY 10021

Laurence R. Young, Ph.D.
Professor
Department of Aeronautics
and Astronautics
Massachusetts Institute of Technology
Cambridge, MA 02139

David S. Zee, M.D.
Professor
Department of Neurology
Johns Hopkins Hospital
Baltimore, MD 21287-6921

Liaison to the National Deafness and Other Communication Disorders Advisory Board

Robert I. Kohut, M.D.
James A. Harrill Professor
and Chairman
Department of Otolaryngology
Bowman Gray School of Medicine
Wake Forest University
Winston-Salem, NC 27103

Resource Persons

Maureen Hannley, Ph.D.
Director of Development and Research
American Academy of Otolaryngology - Head
and Neck Surgery
Alexandria, VA 22314

Michael D. Oberdorfer, Ph.D.
Chief
Strabismus, Amblyopia and
Visual Processing Branch
National Eye Institute
National Institutes of Health
Bethesda, MD 20892-9904

Christopher Platt, Ph.D.
Program Director for Sensory Systems
Directorate for Biological Sciences
National Science Foundation
Arlington, VA 22230

Cynthia M. Shewan, Ph.D.
Senior Vice President for
Research, Analysis, and Development
American Physical Therapy Association
Alexandria, VA 22314

Victor Schneider, M.D.
Space Physiology Program Manager
National Aeronautics and
Space Administration
Washington, D.C. 20546

NIDCD Staff Liaison

Mr. Howard J. Hoffman
Chief
Epidemiology, Statistics
and Data System Branch
National Institute on Deafness and
Other Communication Disorders
National Institutes of Health
Bethesda, MD 20892-7180

Daniel A. Sklare, Ph.D.
Health Scientist Administrator
Division of Communication Sciences
and Disorders
National Institute on Deafness and
Other Communication Disorders
National Institutes of Health
Bethesda, MD 20892-7180

PANEL ON VOICE AND VOICE DISORDERS

Cochairpersons

Gerald S. Berke, M.D.
Professor and Chief
Division of Head and Neck Surgery
University of California at Los Angeles
Medical Center (CHS)
Los Angeles, CA 90024-1624

Jerilyn Ann Logemann, Ph.D.
Professor and Chairperson
Department of Communication
Sciences and Disorders
Professor
Departments of Otolaryngology
and Neurology
Northwestern University
Evanston, IL 60208-3540

Members

Rhoda L. Agin, Ph.D.
Professor
Department of Communicative
Sciences and Disorders
California State University, Hayward
Hayward, CA 94542

Kathryn Albers, Ph.D.
Assistant Professor
Department of Pathology
University of Kentucky
Lexington, KY 40536-0096

Carol Gracco, Ph.D.
Director, Speech and Voice Physiology
Yale University School of Medicine
Department of Surgery - Otolaryngology
New Haven, CT 06511

David G. Hanson, M.D.
Professor and Chairman
Department of Otolaryngology-Head
and Neck Surgery
Northwestern University
School of Medicine
Chicago, IL 60611-3008

Robert E. Hillman, Ph.D.
Director
Voice and Speech Laboratory
Massachusetts Eye & Ear Infirmary
Harvard Medical School
Boston, MA 02114

Ethylin W. Jabs, M.D.
Associate Professor of Pediatrics,
Medicine and Surgery
Center for Medical Genetics
Johns Hopkins University
School of Medicine
Children's Medical and Surgical Center
Johns Hopkins Hospital
Baltimore, MD 21287-3914

Jacqueline E. Jones, M.D.
Assistant Professor
Dept. of Otolaryngology and
Communicative Disorders
New York Hospital- Cornell Medical Center
New York, NY 10021

David P. Kuehn, Ph.D.
Professor
Department of Speech and Hearing
University of Illinois
Champaign, IL 61820-6206

Ying Yong Qi, Ph.D.
Assistant Professor
Department of Speech and
Hearing Science
University of Arizona
Tucson, AZ 85721

Lorraine O. Ramig, Ph.D.
Associate Professor
Department of Communication
Disorders and Speech
University of Colorado
Boulder, CO 80309-0409

Ira Sanders, M.D.
Associate Professor
Department of Otolaryngology
Mt. Sinai School of Medicine
New York, NY 10029

Elaine T. Stathopoulos, Ph.D.
Associate Professor
Department of Communicative
Disorders and Sciences
SUNY at Buffalo
Buffalo, NY 14260

Bettie Steinberg, Ph.D.
Research Director
Department of Otolaryngology and
Communicative Disorders
Long Island Jewish Medical Center
New Hyde Park, NY 11040

Peak Woo, M.D.
Associate Professor
Department of Otolaryngology
Tufts New England Medical Center
Tufts University School of Medicine
Boston, MA 02111

Liaison from the National Deafness and Other Communication Disorders Advisory Board

Byron J. Bailey, M.D.
Wiess Professor and Chairman
Department of Otolaryngology
University of Texas Medical Branch
Galveston, TX 77555-0521

Resource Persons

Bruce R. Gerratt, Ph.D.
Professor
Division of Head and Neck Surgery
University of California at Los Angeles
Los Angeles, CA 90095

Maureen Hannley, Ph.D.
Associate Vice President for
Research and Development
American Academy of Otolaryngology - Head
and Neck Surgery Foundation, Inc.
Alexandria, VA 22314

NIDCD Staff Liaison

Beth M. Ansel, Ph.D.
Health Scientist Administrator
Division of Human Communication
National Institute on Deafness and
Other Communication Disorders
National Institutes of Health
Bethesda, MD 20892-7180

Christy L. Ludlow, Ph.D.
Chief
Voice and Speech Section
Voice, Speech and Language Branch
Division of Intramural Research
National Institute on Deafness and
Other Communication Disorders
National Institutes of Health
Bethesda, MD 20892-1416

Carter Van Waes, M.D., Ph.D.
Acting Chief
Tumor Biology Section
Head and Neck Surgery Branch
Division of Intramural Research
National Institute on Deafness and
Other Communication Disorders
National Institutes of Health
Rockville, MD 20850-3320

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Other Communication Disorders
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NIDCD Information Clearinghouse
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Bethesda, Maryland 20892-3456

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